



## Cohort Study

## Living donor kidney paired exchange: An observational study

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## A B S T R A C T

**Background:** Kidney transplantation is the treatment of choice for patients with end-stage renal disease (ESKD). Kidney paired donation (KPD) provides the chance to match an incompatible donor/recipient pair with another donor and recipient in a similar condition. We aimed to compare the outcomes of pair exchange kidney transplantation with traditional live donor kidney transplantation in our context.

**Method:** A review of medical records of 62 patients (31 pairs) who underwent two-way conventional living kidney pair exchange from July 2016 to June 2021 was done. The control group was considered those 62 patients who had undergone classic live donor kidney transplantation (LDKT) during the study period. The patient's demographics, intraoperative and postoperative variables including delayed graft function, length of hospital stay, graft survival, patient survival, and rejections rates were compared between the groups (KPD and LDKT).

**Results:** The majority of recipients were male (77.4 and 80.6%) while donors were female (77.4 and 69.4%) in KPD and the LDKT groups. Mean ages were 37 years (range: 19–59) and 37 years (range: 17–65) for the recipient's in KPD and the LDKT. KPD transplantation was performed in 62 recipients to avoid blood group incompatibility. There were no significant differences in outcomes comprising delayed graft function (1.6 and 3.2%), graft survival (100% in both groups), patient survival (95.2 and 96.8%), and rejections rates (1.6 and 1.6%) between KPD and LDKT group ( $P > 0.005$ ). The length of stay was similar (5.9 and 5.7 days) in KPD and LDKT groups ( $P > 0.005$ ).

**Conclusions:** The outcomes of KPD were comparable with classic LDKT in terms of delayed graft function, length of hospital stay, graft survival, patient survival, and rejections rates in our study. Therefore, the kidney paired donation program should be encouraged and promoted in centers where the ABO-incompatible transplant is expensive with added risk and the rate of deceased donor transplantation is very low.

## 1. Introduction

Chronic kidney disease is a global health problem with various range of prevalence rates (11%–13%) [1]. Kidney transplantation is the treatment of choice for patients with end-stage renal disease (ESKD). It has several benefits over dialysis in all age groups in terms of quality of life, mortality, and life expectancy [2]. The global shortage of deceased donor organs has made a high level of dependence on a living kidney donation program [3]. While comparing living donor kidney transplantation to deceased donor transplantation; has superior long-term results with graft survival may be due to less dialysis waiting for time or avoidance of dialysis [4].

Classic living donor kidney transplantation was done effectively for the first time in Nepal in 2008 [5]. Interestingly, Shahid Dharmabhakta National Transplant Centre, Bhaktapur, Nepal (SDNTC) transplant team has performed more than 800 kidney transplantations to date. Moreover, the most of these transplants were living related donor

transplantations, followed by 62 living kidney donor kidney pair exchange, and only six of all were brain-dead donor kidney transplantations. Furthermore, SDNTC had performed its first live donor pair exchange kidney transplant in July 2016. Kidney paired donation (KPD) is an alternative approach to overcome different incompatibilities including human leukocyte antigen (HLA), ABO blood group, immunological, chronological, and financial incompatibilities that allow a medically suitable but incompatible pair to exchange kidneys with one or more other incompatible pairs so that all recipients receive compatible organs from strangers [6,7]. We aimed to compare the outcomes of pair exchange kidney transplantation with traditional live donor kidney transplantation in our context.

## 2. Materials and method

This was a retrospective cross-sectional, quantitative, observational single centre study of 62 kidney paired donation transplantations from

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July 2016 to June 2021 at Shahid Dharmabhakta National Transplant centre, Bhaktapur, Nepal. The kidney transplantation was performed to avoid blood group incompatibility in all these patients. The data was compared with that of 62 patients who had undergone classic live donor kidney transplantation during the study period. The study was approved by the Institutional Review Committee of National Health Research Council, Kathmandu, Nepal (687/2021). The inclusion criteria were set as those patients who underwent two-way live donor pair exchange kidney transplantation and the same numbers of control groups who underwent traditional living kidney donation transplantation during the study period. We divided the patients into two groups based on the pair exchange group and the traditional living-related kidney transplantation group. We compared demographics, perioperative variables, and outcomes including short-term graft survival, patient survival, and rejections rates of KPD groups with those of the LDKT group. All the patients underwent a complete pre-operative evaluation to obtain comparable pairs from a functional, anatomical, and immunological perspective.

Induction immunosuppressive therapy was achieved with methylprednisolone and rabbit-anti thymocyte globulin (r-ATG) in all patients. While Maintenance immunosuppression consisted of prednisolone, calcineurin inhibitor (CNI) tacrolimus, and mycophenolate mofetil. The doses of mycophenolate were adapted according to complete blood counts. The doses of tacrolimus were adjusted based on serum tacrolimus levels considering the target of 8–10 ng/mL. Valganciclovir was given as infection prophylaxis for cytomegalovirus and trimethoprim-sulfamethoxazole was given for *Pneumocystis Carinii*. Delayed graft function (DGF; defined as the need for dialysis within the first week of transplantation), acute rejection incidence (AR), tendencies in serum creatinine, and graft and patient survival rates were compared between the groups. Renal graft biopsy was implemented in cases of acute graft dysfunction and succeeded according to standard guidelines.

Our work is fully compliant with the STROCSS criteria [www.strocsguideline.com](http://www.strocsguideline.com) in which a completed STROCSS checklist stating the page numbers [8].

### 3. Results

Out of 124 live donor kidney transplantations, 62 patients were KPD and 62 patients were classic LDKT. The majority of recipients were male (77.4 and 80.6%) while donors were female (77.4 and 69.4%) in KPD and the LDKT groups. Mean ages were 37 years (range: 19–59) and 37 years (range: 17–65) for the recipient's in KPD and the LDKT groups. The patient's demographics and perioperative data are shown in Table 1. Basic demographic data were similar between the KPD group and the LDKT group ( $P > 0.005$ ) as shown in Table 1. The median follow-up was 6–60 months.

Primary disease-causing of ESRD was primarily hypertension ( $n = 20$ ) (Table 1). Most of our recipients are from Bagmati province (Table 1). The intraoperative and postoperative variables are shown in Table 2. Graft survival was 100% in both groups whereas patients survival was 95.2 and 96.8 in KPD and LDKT groups respectively. However, the difference was not significant between the groups. The cause of mortality in these patients was not due to primary graft failure rather it was due to COVID-19 infections in all these patients. Table 2 also shows graft function in terms of the mean serum creatinine level of the two groups during the follow-up period. Our total of three patients experienced delayed graft function as defined by the need for dialysis in the first week where one patient from the KPD group and two patient from LDKT group. There was biopsy-proven acute graft rejection observed in one patient (1.6%) in both the groups. We did not observe any events of hyperacute rejection. All acute rejections were recovered after acute rejection treatment with pulse methylprednisolone.

**Table 1**  
Patient's demographics and perioperative data.

Variable	KPD N = 62 (%)	Classic LDKT N = 62 (%)	P value
Recipient's Age, (years) range	19–59	17–65	0.471
Age, (years) Mean $\pm$ SD <sup>♦</sup>	37.6 $\pm$ 9.4	37 $\pm$ 11.7	
Sex			0.659
Male	48 (77.4)	50 (80.6)	
female	14 (22.6)	12(19.4)	
Comorbidity,%			0.335
Diabetes mellitus	7 (11.3)	9 (14.5)	
Hypertension	20 (32.3)	20 (32.3)	
PCKD <sup>*</sup>	0 (0)	3 (4.8)	
Other	12 (19.4)	7 (11.3)	
Pre-transplant Dialysis			0.559
Yes	60 (96.8)	61 (98.4)	
No	2 (3.2)	1 (1.6)	
Address	12 (19.4)	13 (21.0)	0.474
Province 1	4 (6.5)	5 (8.1)	
Province 2	26 (41.9)	20 (32.3)	
Bagmati	6 (9.7)	9 (14.5)	
Gandaki	11 (17.7)	10 (16.1)	
Lumbini	2 (3.2)	0 (0)	
Karnali	1 (1.6)	3 (4.8)	
Sudur Paschim	0 (0)	2 (3.2)	
India			
Donor			0.590
Age, (years) range	20–56	22–68	
Means $\pm$ SD	39.3 $\pm$ 8.7	41.5 $\pm$ 11.8	
Donor Sex			0.310
Male	14 (22.6)	19 (30.6)	
Female	48 (77.4)	43 (69.4)	
PRA			0.857
I	10.4 $\pm$	10.1 $\pm$ 12.1	
II	12.6	12.5 $\pm$ 13.6	
	12.4 $\pm$		
	13.2		

Continuous variables are used as mean  $\pm$ SD, Categorical variables are used as n (%); <sup>\*</sup>PCKD; Polycystic kidney disease, <sup>†</sup>PRA; Panel reactive antibody, <sup>♦</sup> SD; Standard deviation, \* P; value is significant if  $< 0.05$

**Table 2**  
Intraoperative and postoperative data.

Variable	KPD N = 62 (%)	Classic LDKT N = 62 (%)	P value
CIT <sup>†</sup>	70.6 $\pm$ 24.1	70.6 $\pm$ 25.6	0.857
WIT <sup>*</sup>	32.6 $\pm$ 6.5	32.8 $\pm$ 7.0	0.990
DGF <sup>♦</sup>	1 (1.6)	2(3.2)	0.500
Rejection	1 (1.6)	1 (1.6)	0.752
Length of hospital stay of recipient (days)	5.97 $\pm$ 0.78	5.7 $\pm$ 0.77	0.464
First year Creatinine (mg/dl)	0.94 $\pm$ 0.24	0.91 $\pm$ 0.20	0.990
Third year Creatinine (mg/dl)	0.96 $\pm$ 0.24	0.91 $\pm$ 0.24	0.407
Five year Creatinine (mg/dl)	0.93 $\pm$ 0.23	0.91 $\pm$ 0.20	0.990
Survival	59 (95.2)	60 (96.8)	0.648

<sup>†</sup>CIT; Cold ischemia time, <sup>\*</sup>WIT; Warm ischemia time (second), <sup>♦</sup>DGF; Delayed graft function

### 4. Discussion

Kidney paired donation (KPD) provides the chance to match an incompatible donor/recipient pair with another donor and recipient in a similar condition [9]. Both kidney paired donation (KPD) and desensitization are alternatives for patients with incompatible donors. Approximately 54% of living donor-recipient pairs could not able to have LDKT due to ABO blood group incompatibility or pre-existing

donor-specific antibodies (DSA) to human-specific leukocyte antigen (HLA) [10]. Numerous different modalities have been established to overcome these different immunological barriers. For ABO-incompatible transplantation, a long-term better outcome can be achieved by removal of anti-blood group antibody using plasmapheresis or specific immunoabsorption, rituximab, and long-term standard immunosuppression [11]. However, while for HLA-incompatibility in the presence of preformed DSA resulting in positive cell-based cross-match is still related to high rates of antibody-mediated graft rejection, and short-term and long-term graft failure [12]. Despite desensitization treatments that have been utilized to accomplish transplantation from an incompatible donor, such processes are expensive and might have related complications and inferior long-term consequences in comparison to KPD [13].

Kidney exchange transplantation is a fast-rising modality for allowing living associated donor kidney transplantation (LDKT) for patients who are incompatible with their healthy, willing, and living donors [14, 15]. It is also more suitable in countries where deceased donor kidney transplantation rates and ABO-incompatible transplantation are not available or are very low [16]. HLA matched KPD needs less immunosuppression and fewer costs, lower infective problems and good survival, mainly in developing countries like ours [17]. Thus, KPD is a significant source to rise in the donor pool to avoid profitable transplantation [14]. Kidney exchange transplantation offers good quality organs and is highly used in developed and developing countries [18]. KPD is more cost-effective due to its comparatively short waiting time than remaining on long-term maintenance dialysis [19]. The limitations in going through an effective maintenance dialysis program make renal transplantation the only feasible alternative for patients with ESRD in developing countries like ours.

Pair exchange kidney donation has grown from the classic concurrent anonymous two way kidney exchange to more multifaceted methods (3-way, 4-way, and n-way exchanges) [20]. The commonly paired exchange kidney donation is a closed loop of two-way kidney exchange in which the first pair (A patient and B donor) exchanges the kidney with the second pair (B patient and A donor) and both the pairs are benefitted resulting in two compatible kidney transplantation [21]. Meanwhile, a study mentioned the 3-way exchange rises match rate up to 66% [22] and is the most ideal length of kidney paired donation to reach a good match rate and to practice concurrent kidney transplantation especially for newly starting single centre kidney paired donation programs [23]. Multiple programs around the world have used variations of the exchanges [21,24]. The conventional KPD was the common type of pair exchange performed in our centre. The term “conventional balanced” is a type of KPD transplant in which blood type A and B donor/recipient is matched to a pair with the opposite incompatibility. Moreover, Conventional unbalanced is applied in which a donor-recipient pair is compatible, but not identical (O donor and A recipient) approves to exchange with a donor-recipient pair who are ABO-incompatible (A donor and O recipient). However, “Unconventional paired” is applied when donor-recipient pairs are incompatible because of a positive crossmatch. This provides donors and recipients with blood groups O and AB to participate in the exchange [21].

In this study, The majority of recipients were male while donors were female in both groups similarly reported in the literature [25]. The mean age of the recipient was  $37.6 \pm 9.4$  (range 19–59) years, and for donors, it was  $39.3 \pm 8.7$  (range 20–56) years in our KPD patients. The benefits of having an LDKT from a donor who is younger vs. elderly are arguable [26].

The outcomes in terms of delayed graft function, length of hospital stay, graft survival, patient survival, and rejections rates were similar between the KPD and LDKT groups and these findings are comparable with other studies [27]. One study described 11 compatible pairs who participated in KPD, along with the recipients’ 11 matched, exchange donors with similar results to ours [28]. Another study has mentioned 17 compatible pairs among 134 total KPD over 3 years [29]. Most of our

compatible pairs joined in internal exchanges within our centre rather than in external exchanges with other centers via multi-centre KPD registries.

The greatest challenge to KPD’s success is what is called ‘the balkanization of the patient pool’. The meaning of this term is that transplant centers and pairing organizations operate independently of one another, preventing matches that could potentially exist between patient pools [30]. In our context, the patient and their family are the ones who are finding candidates for pair exchange through personal contact. The institution is only taking part in verification, and assistance of the process and transplant procedure. Furthermore, currently, we do not have international collaboration, however advocacy for the process of collaboration has started nationally to increase the patient pools. The troubles faced in expanding KPD in Nepal consist of the absence of a national record for incompatible pairs, absence of coordination between transplant centers, feasible human leukocyte antigen (HLA) laboratories, differences in policies across diverse transplant centers about candidate selection, manual allocation, and absence of classy computer systems to increase match rates. Similar challenges have been mentioned in a study from India [20]. Other things, there is a notable absence of knowledge among the people about KPD. To improve the situation, all the patients on maintenance dialysis should be encouraged about the practicability and cost-effectiveness of KPD when an ABO-incompatible healthy and eager donor is available. The renal transplantation program in developing countries like ours is also facing varieties of difficulties including poor public health systems with low insurance coverage leading to self-health expenditure and inaccessibility. Therefore, a procedure like KPD is cost-saving and has a decreased waiting time, it could be applied to a country like ours.

We believe that this is one of the specific series clearly showing the comparable outcomes of KPD and LDKT in our context. Regarding the limitations of our study, we acknowledge that this is a retrospective and single-centered study. Hence, to validate our findings, we recommend directing properly planned prospective studies in our setting in the future.

Conclusions: The outcomes of KPD were comparable with classic LDKT in terms of delayed graft function, length of hospital stay, graft survival, patient survival, and rejections rates in our study. Therefore, the KPD program should be encouraged and promoted in centers where the ABO-incompatible transplant is expensive with added risk and the rate of deceased donor transplantation is very low.

### Ethical approval

The study was approved by the Institutional Review Committee of Nepal Health Research Council, Kathmandu, Nepal (687/2021).

### Funding

There are no sponsors involved in the study.

### Author contribution

All authors equally contributed to the study concept or design, data searching, data analysis or interpretation, writing the paper.

### Registration of research studies

1. Name of the registry: <http://www.researchregistry.com>
2. Unique Identifying number or registration ID: 7776
3. Hyperlink to your specific registration: <https://www.researchregistry.com/browse-the-registry#home/>

### Guarantor

Dr. Pukar Chandra Shrestha.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Annals of medicine and surgery

The following information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

### Consent

Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

Authors must obtain written and signed consent to publish a case report from the patient (or, where applicable, the patient's guardian or next of kin) prior to submission. We ask Authors to confirm as part of the submission process that such consent has been obtained, and the manuscript must include a statement to this effect in a consent section at the end of the manuscript, as follows: "Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request".

Patients have a right to privacy. Patients' and volunteers' names, initials, or hospital numbers should not be used. Images of patients or volunteers should not be used unless the information is essential for scientific purposes and explicit permission has been given as part of the consent. If such consent is made subject to any conditions, the Editor in Chief must be made aware of all such conditions.

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Is a retrospective study. So Not applicable.

### Declaration of competing interest

No conflict of interest.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103761>.

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