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Case Report

Kidney transplantation from brain-dead donors in Nepal: Report of first six cases

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ABSTRACT

Introduction: and importance: Kidney transplantation is one of the best treatment options for patients with end-stage renal disease. More than 90% of patients awaiting renal transplantation die without getting the kidney for transplantation. Brain dead donor kidney transplantation can bridge this gap proficiently. We aim to report details of the first six patients who had undergone brain-dead donor kidney transplantation in the history of transplantation in Nepal.

Case presentation: We conducted a descriptive analysis of clinical data of six adult recipients with kidney transplantation from three brain-dead donors. We described postoperative complications, length of stay, graft function which was documented with serum creatinine, acute rejection episode, delayed graft function, and patient/graft survival of recipient. Recipients were between 15 and 56 years old. Three patients experienced delayed graft function. Urinary tract infection was observed in two patients, both of whom were treated with antibiotics. One patient had acute graft rejection. None of our patients required reoperation. Length of hospital stay ranged from 9 to 32 days. The postoperative graft function was 100% in all patients. There was no graft loss, and no death was observed during follow-up.

Clinical discussion: Following the initiation of the brain-dead donor transplantation program, a lot of work needs to be done to make it a regular practice. Thus, this program needs support from all sections of society and government. This can be the only solution to decrease the huge gap between the supply and demand of organs in Nepal.

Conclusion: This case reports indeed revealed impressive success in initiating a brain-dead donor kidney transplantation program in a developing country that in terms of quality, meets comprehensive standard with acceptable graft function and patient/graft survival in under limited resources healthcare setting.

1. Introduction

Renal transplantation (RTx) is the best treatment modality for end-stage renal disease (ESRD). Renal transplantation has superior outcomes over other therapy such as dialysis in terms of health economics as well as improved long-term survival, quality of life, and productivity [1,2]. More than 90% of patients awaiting renal transplantation die without getting the kidney for transplantation. Brain dead donor kidney transplantation can bridge this gap proficiently [3]. There are no national statistics on the incidence of renal failure in Nepal. However, based on the 3 million cases of diabetes in Nepal, it is estimated that there are 3000 cases of renal failure in line with global statistics [4]. Moreover, there is a lack of data on the percentage of people who can gain access to renal replacement therapy.

The first live donor kidney transplantation was performed successfully in Nepal in 2008 [5]. In the meantime, nine years after the effective start of kidney transplantation, the first brain dead-donor organ transplant was performed in Nepal-creating history at Shahid Dharmabhakta National Transplant center (SDNTC) on May 11, 2017. At that time, two patients received a kidney each from a brain-dead donor, and both

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recipients had successful admirable results. Only four more brain-dead kidney donations have been done at SDNTC till now. In addition, no other transplant hospital in Nepal has been able to begin brain-dead donor transplantation yet.

This lack of expansion of the brain-dead donor transplant program is disheartening especially when there are organs available from brain-dead donors and there are regulations in place to enable the use of these organs. More specifically, over 2000 people die in road traffic accidents every year in Nepal [6]. Different organs can be acquired from deceased individuals for transplantation which could save many lives of organ failure patients. Although the brain death donation law in Nepal was established in 2016, the expansion of the brain dead donor kidney transplantation program has been slower than expected. This might be due to legal, social, religious, spiritual, political, socioeconomic, medical, and ethical issues [7,8]. Thus, examining the factors that prevent increasing deceased organ donation in Nepal remains a big challenge and must be done to successfully expand the program.

In the meantime, considering the depth of this issue, we aim to report details of the first six patients who had undergone brain-dead donor kidney transplantation in Nepal. This will add up some bricks to the literature regarding brain-dead donor kidney transplantation in our context where we still lack literature. We report these cases in line with the updated consensus-based surgical case report (SCARE) guidelines [9].

2. Report of cases

A total of six patients who underwent kidney transplantation from three brain-dead donors at Sahid Dharmabhakta National Transplant centre (SDNTC), Nepal were included. The team leader (P·C·S.) had higher surgical training in the United Kingdom with more than 15 years of experience in transplant surgery. Some of the members of the team had a formal fellowship in kidney transplant surgery and other members of the team were trained by P·C.S. . All transplantations were performed as emergency surgeries following the sudden availability of brain-dead donors. All organs were transplanted to ABO-identical recipients. All recipients had regular hemodialysis before transplantation. All of our recipients were male with ages ranging from 15 to 56 years. The demographic characteristics of patients and perioperative data are shown in Table 1. The consent for organ donation in all brain-dead donors was provided by their relatives. Out of three donors, one patient had died in a road traffic accident, one had a stroke, and the third one had a fall from stairs. The procurement site of our hospital was nearby. This helped in the maintenance of the minimum cold ischemia time. All donors were hemodynamically stable. Range of donor age 30–72 years.

Regarding operative techniques, the donor's kidneys were procured by a team of transplant surgeons and anesthetists. The abdomen was opened with a midline incision. The duodenum and right colon were mobilized, showing the great vessels. The aortic bifurcation was identified. The ligation of inferior mesenteric vessels was performed. Cannulas were put in situ for cooling and flushing. The ureters were ligated and divided into their distal part. The kidneys were removed en bloc with the vena cava and aorta. Kidneys were placed in a Histidine-Tryptophan-Ketoglutarate (HTK) solution for preservation and transport. Transplant procedures were done using the usual technique in the right or left iliac fossa. Most of our donor patients had a single renal artery except one who had three renal arteries. Lick Gregoir's method was used to create ureteroneocystneostomy and a double-J ureteral catheter was put in (Table 1).

All recipient patients were given methylprednisolone and rabbit-anti-thymocyte globulin (r-ATG) as an induction immunosuppressive therapy. While, prednisolone, a calcineurin inhibitor (CNI), and mycophenolate mofetil were included in Maintenance immunosuppression. The doses of mycophenolate were managed based on complete blood counts. The doses of tacrolimus were adjusted according to serum tac levels (8–10 ng/mL). Valganciclovir was commenced for cytomegalovirus and trimethoprim-sulfamethoxazole was given for Pneumocystis Carinii pneumonia as infection prophylaxis.

All the postoperative outcomes were documented. Delayed graft function (DGF) which is defined as the need for dialysis within the first week of transplantation), graft function with tendencies in serum creatinine, acute rejection incidence (AR), and graft and patient survival rates were considered during follow-up (Table 2). Renal graft biopsy was performed in cases of acute graft dysfunction. Instantaneously after transplantation, all patients had decent graft reperfusion intraoperatively and immediate urine output was adequate in all patients. Prophylactic anticoagulation during hospitalization was given to all recipients. An early graft Doppler ultrasound (DUS) was accomplished in all patients before discharge. Decent flow in the grafts, good patency of the anastomoses, and absence of signs of intraluminal thrombi were noticed. Delayed graft function was found in three patients needing 2–3 dialysis periods until hospital discharge. Urinary Infection was found in two patients, and both were treated with antibiotics. Patient 4 developed an acute rejection of graft (confirmed by kidney biopsy) which was

Table 1
Demographics and Perioperative data.

Recipient	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Recipient's Age (Years)	51	15	56	30	40	31
Sex	Male	Male	Male	Male	Male	Male
Weight (kg)	72	41	69	51	66	66
Blood Group	O Positive	O Positive	O Positive	O positive	O Positive	B Positive
Medical illness	DM/HTN	HTN	HTN/ADPKD	HTN	HTN	HTN
Dialysis access	AVF	AVF	AVF	AVF	AVF	AVF
History of Prior dialysis	Yes	Yes	Yes	Yes	Yes	Yes
Donor Age (years)	30	30	72	72	32	32
Donor Sex	M	M	M	M	M	M
Donor type	Deceased	Deceased	Deceased	Deceased	Deceased	Deceased
Donor blood group	O Negative	O Negative	O Positive	O Positive	O Negative	O Negative
Cold ischemia time (hours)	5	5	4	4	4	4
Second warm ischemia time surgery (mins)	47	38	46	54	72	44
No. of Artery	1	1	1	1	3	1
Arterial anastomosis	IIA	CIA	IIA	IIA	EIA	IIA
Ureterocystostomy	Lick Gregoir's technique	Lick Gregoir's technique	Lick Gregoir's technique	Lick Gregoir's technique	Lick Gregoir's technique	Lick Gregoir's technique
Induction therapy	ATG	ATG	ATG	ATG	ATG	ATG
Maintenance therapy	Tac, MM, Steroid	Tac, MM, Steroid	Tac, MM, Steroid	Tac, MM, Steroid	Tac, MM, Steroid	Tac, MM, Steroid

DM; Diabetes mellitus, HTN; , Hypertension, PKD; Polycystic kidney disease, AVF; arteriovenous fistula, IIA; Internal iliac artery, CIA; Common iliac artery; EIA; External iliac artery, ATG; Antithymocyteglobulin, Tac; Tacrolimus, MM; Mycophenolate moefetil

Table 2
Postoperative data.

Recipient	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Reexploration	None	None	None	None	None	None
Biopsy	None	Yes-ATN	Yes-ATN	Yes-Acute rejection	Yes- ATN	None
Delayed graft function	No	Yes	No	No	yes	Yes
Rejection	No	No	No	Yes (acute)	No	No
POD Dialysis (No.)	–	2	–	–	3	2
Infectious complication	None	None	None	None	UTI	UTI
Vascular Complication	None	None	None	None	None	None
Length of Hospital stays (days)	9	23	14	21	32	32
No. of transplatation	1	1	1	1	2	1
Creatinine POD1	5.7	3.5	4.3	5.9	10.8	8.7
Cr POD7	1.3	2.6	2.4	2.6	11.2	7.8
Cr during discharge	1.4	1.1	1.9	1.6	1.9	1.8
Cr POD 1year	1.1	1.0	1.9	1.1	1.1	1.0
Cr POD 3 year	1.0	0.9	2.1	1.1	0.9	1.0
Cr POD 4 year	1.1	1.1	–	–	–	–
Current Creatinine	1.1	1.0	2.2	1.2	1.0	1.1
Duration from Operation	4.5 Years	4.5 Years	3 Years	3 Years	3 Years	3 Years
Graft loss	None	None	None	None	None	None
Recipient's Death	No	No	No	No	No	No

ATN; Acute tubular necrosis, POD; Postoperative day, Cr; Creatinine.

managed with pulse methylprednisolone therapy (500 mg for 3 days).

The length of hospital stay ranged from 9 days to 32 days. One of the patients had an uneventful postoperative course while 3 patients developed delayed graft function; one had acute graft rejection and one had urinary tract infection leading to the variable length of hospital stay. All the patients were followed up regularly after discharge. Satisfactory outcomes with no other complications, loss of grafts, or deaths, and good renal function based on the measurement of serum creatinine levels were noted during follow-up. All recipients are leading a normal life with adequate immunosuppressive therapy. They have been followed up for a minimum of three years to a maximum of four and half years. The graft survival and patient survival were 100% during the follow-up period. The post-transplantation data of our patients has been shown in Table 2.

3. Discussion

SDNTC was established in 2012 to establish an accessible organ transplantation program in Nepal and has performed 900 kidney transplants to date, and acts as the Coordination center for cadaveric organ transplantation. However, most of these transplants have been living donor transplants, with 62 patients having received their transplantation through living kidney donor pair exchange, and only six of all transplants were brain dead donor kidney transplantation [10,11]. Although significant strides have been made in the field of transplantation in Nepal, there is a potential to grow the deceased donor program to mitigate the shortage of organs and to meet the transplant needs of the population. Therefore, in this paper, we describe the first six brain-dead donor kidney transplants done in Nepal and demonstrate that these six transplants resulted in successful outcomes for the patients post-op and during follow-up. These results provide evidence for the success of cadaveric donor transplantation in Nepal and suggest a potential for expansion of the deceased donor transplantation program.

Setting up brain dead donor kidney transplantation program in a country like Nepal, where kidney transplantation was in its initial stages and amidst the lack of trained human resources and infrastructures, was a huge challenge. In addition, medical staff and the general population lacked awareness of the advantages of brain-dead donor kidney transplantation. Moreover, religiousstigmata, misconceptions, and false traditional beliefs about organ donation created problems in starting deceased donor kidney transplantation in Nepal like in other developing countries [7]. Nevertheless, with the persistent efforts of the transplant team, the dream became reality.

There are various significant challenges in scaling up the cadaveric donor program. These challenges range from lack of awareness to sociocultural reasons. Lack of public awareness is usually mentioned as the cause for not commencing cadaveric organ donation of vital organs from brain-dead patients in Nepal. Most people are not aware of brain-dead organ donation for transplantation. Another common challenge is sociocultural tradition. It is not an easy procedure. People whose relatives die or are declared brain-dead will not simply let you obtain organs from their relative's dead bodies. Many families even have religious false beliefs. They cannot accept the idea that the body of their relative will be cut to get organs for transplantation similarly mentioned in the literature [3].

Although studies have shown that compared to deceased donor kidneys, live donor kidney transplants experience a higher success rate, as well as a longer life span of the transplanted organ, deceased organ donations allow usage of multiple organs which would otherwise have been wasted [12]. Brain-dead organ donation is also without donor risk as well as potential long-term organ failure due to lack of reserve. WHO data shows that brain-dead organ donation is practiced in only about 75 countries in the world being more common in economically developed countries [13].

Effective deceased organ donation and retrieval need appropriate legislation and government logistical support. There are several models to establish the diagnosis of a deceased donor, organ procurement, and allocation to perform deceased donation transplantation in different countries in the world [11]. Some countries have come up with legal organ donation after brain death or circulatory arrest [14]. The procurement rate of organs from patients with cardiac death is very low in comparison to the brain death donor [15]. Moreover, common aspects of different organ procurement units in different countries are the presence of a national center for effective coordination and centralized organ allocation, the organization of a network of independent organ procurement units covering defined geographical areas of the country, and several transplant centers serving many connected hospitals in a particular geographic area. They are managed by well-trained and motivated coordinators and funded centrally by the government. Nepalese parliament had made some important modifications to human organ transplantation regulation and prohibition act 1998 in 2016 [5]. It extended the living donor pool, and legalized organ donation through pair exchange. The most significant footstep was the legalization of the brain-dead donor transplant. The aim of modification is to increase the number of essential transplants, to reduce the overall cost of the transplant technique, and number of possible recipients travelling to other countries for transplantation. The new legislation makes it mandatory to the treating hospitals to formally declare brain death. However, this is

yet to be put into practice by the hospitals in Nepal. To increase the donor pool, a system of national registry should be made functional and maintained. Public awareness to organ donation should be increased by educating the school children. Government backed health insurance program could incentivize public to become an organ donor by allowing reimbursements to people who sign up to organ donation. Driving license application should have a check box to become organ donor. Government aided schemes such as Bipanna can be modified to incentivize organ donors such that those who sign up to organ donation will have higher amount of state funding in case they develop serious illness covered by the scheme.

To be a recipient of cadaveric organs the patient must be registered and placed on the waiting list by the coordination unit which is currently SDNTC. The patient has to undergo a formal assessment and make a formal application in a prescribed format. The process of brain-dead organ donation is regulated legislation. Accordingly, the first step to brain dead organ donation is to declare that the patient has sustained brain death. The hospital which declares brain death has to have minimal facilities specified by the law such as the presence of anesthetist/intensivist, at least two ventilators, ICU with at least two monitored beds, operation theatre, CT scan, arterial blood gas facilities, etc. The brain death test has to be performed by the concerned specialist and anesthetist/intensivist on two occasions. The test is done in three stages namely preliminary examination, brain stem test, and apnea test. Once the brain death is confirmed it has to be declared in a specified form [16]. Now the formal consent for donation can be signed by the relatives. Once the center is informed coordinators and transplant teams will visit the hospital to assess the donor. If a donor is suitable the transplant team will assist in donor management and subsequently transfer the patient to the operating theatre for organ harvesting. The chosen recipients are admitted to the hospital and kept ready for the surgery while the organ is being transported.

The organs prioritization process is quite clear. There is a large number of potential transplant recipients compared to a very meager supply of deceased donor organs. Hence a system of prioritization has been defined by the regulation based on several internationally accepted factors. For example, for kidney allocation, the scorings are based on factors such as duration of time on the waiting list, time since dialysis, human leucocyte antigen (HLA), panel-reactive antibody (PRA), donor-specific antibody (DSA), complement-dependent cytotoxicity (CDC) matching, age difference, and sex. The latter was introduced to remove the gender bias favoring male patients seen widely in practice [17,18]. Thus, male patients are awarded a score of 1 whereas female patients get a score of 3 out of a maximum of 42. This kind of scoring has been provisioned to address gender-based biases in live donor kidney transplantation in Nepal which goes heavily in favor of males.

Looking at the final results of our series, there was no loss of graft as well as no loss of a patient in 1, 3, and 4 years of follow-up post-operatively. Patient's graft function along with graft and patient survival outcomes in this series were compared with existing literature [7,19].

We also acknowledge that being a retrospective single-center evaluation with only six cases a limitation of this series. However, brain-dead donor kidney transplantation can expand the donor pool and decrease the waiting list for kidney transplantation, mainly in a developing country like ours. This is the first series from our country which demonstrates brain-dead donor kidney transplantation can give satisfactory outcomes, encouraging the practice of this method across the country.

4. Conclusions

Following our initiation of brain-the dead donor transplantation program, a lot of work needs to be done to make it a regular practice. Thus, this program needs support from all sections of society and government. This can be the only solution to decrease the huge gap between the supply and demand of organs in Nepal. These case reports indeed showed impressive success in initiating a brain-dead donor kidney transplantation program in a developing country that in terms of quality meets comprehensive standards with acceptable graft function and patient/graft survival in under limited resources healthcare setting.

Ethical approval

Is a case reports, informed consent has been given by all adult patients and for a minor patient, his parents have given written informed consent for publication.

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Author contribution

TRB involved in the study concept, data collection, writing of manuscript and final decision to publish. While PCS, MD, RKV and KKS involved in the study concept, critical revision of manuscript and final decision to publish.

Trail registry number

Not applicable.

Guarantor

Dr. Tika Ram Bhandari.

Consent for publication

Written informed consent was obtained from all adult patients and for a minor patient, his parents have given written informed consent 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.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104386.

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