DECEASED DONOR KIDNEY TRANSPLANTATION: A RETROSPECTIVE ANALYSIS FROM A TERTIARY CARE HOSPITAL IN MUMBAI

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ABSTRACT

BACKGROUND

Increasing deceased donor kidney donation is the only answer to fill the large gap between availability and need for organ donors. Deceased donor kidney transplant rates are picking up in the Southern and Western regions of India and there is a need to look at the outcomes at various institutes and share the experience.

The objective of the study is to evaluate outcomes of deceased donor kidney transplants (DKT) done at a tertiary care centre in Mumbai.

MATERIALS AND METHODS

In this retrospective study, outcomes of all DKTs done from April 2012 to July 2017 were evaluated. Induction immunosuppression consisted of two to three doses of anti-thymocyte globulin (1.5 mg/kg per dose) and methylprednisolone pulses whereas maintenance immunosuppression regimen consisted of prednisolone, mycophenolate mofetil and tacrolimus. The data was analysed for demographic profile of recipients and donors, comorbidities in recipients, cause of kidney disease in recipients, waiting period on dialysis, delayed graft function, episodes of rejections, induction agents used, maintenance immunosuppressants, infection episodes, patient and graft survival and causes of death.

RESULTS

A total of 21 DKTs (52.4% male recipients) were performed during the study period. The mean (+ SD) age of recipients and donors was 46.71 (±10.6) and 47.8 (+13.5) years respectively. Incidence of biopsy proven acute cellular rejection was 9.5%. Patient survival at one, three and five years were 90.5%, 84.5% and 84.5% respectively. Four (19.04%) grafts were lost during the study period, three grafts were lost because of death of the patients (two at three months and one at 22 months post-transplant) and only one other graft was lost at 43 months with patient returning to dialysis. Three patients (14.3%) died during the study period; two due to sepsis and one due to cardiovascular disease.

CONCLUSION

Current study results suggest that DKT can be successfully carried out with good results even with the current limitations.

KEYWORDS

Deceased Donor, kidney transplant, survival, dialysis.

HOW TO CITE THIS ARTICLE: Bichu S, Tilve PV, Billa V, et al. Deceased donor kidney transplantation: a retrospective analysis from a tertiary care hospital in Mumbai. J. Evid. Based Med. Healthc. 2018; 5(35), 2546-2549. DOI: 10.18410/jebmh/2018/525

BACKGROUND

Kidney transplantation is the best option for patients with end stage kidney disease (ESKD).[1] However, non-availability of live related donors is a major impediment for kidney transplants. This is because of small nuclear families, incompatible blood groups, presence of diabetes, hypertension and other comorbidities in prospective donors and unwillingness to donate. ESKD patients, hence, have no option but to rely on deceased donors to undergo kidney transplant. However, in Mumbai, the waiting time from registration to getting a kidney is very long because of the huge demand-supply gap. From January 2001 to March 2018, only 632 transplants have been performed in Mumbai whereas there are more than 1000 patients on the city waiting list.[2] In India, less than 5% of the total renal

Financial or Other, Competing Interest: None.
Submission 07-08-2018, Peer Review 10-08-2018,
Acceptance 20-08-2018, Published 22-08-2018.
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DOI: 10.18410/jebmh/2018/525

transplants of about 3500 per year are deceased donor renal transplants (DKT).[3]

Fortunately, DKT is now achieving momentum in India particularly in the Western and Southern states.[4] The formation of National Organ and Tissue Transplantation Organization (NOTTO) by the Government of India, has given a fillip to the program and will make it organized and robust in times to come.[5] Apart from the issues faced in increasing the number of donations and organ distribution there are currently certain shortcomings such as acceptance of extended criteria donors (ECD), bypassing human leucocyte antigen (HLA) tissue matching, reliance only on complement-dependent cytotoxicity (CDC) crossmatch and poor general health of most recipients at the time of transplant. These shortcomings are expected to affect the clinical results.

There is published data on outcomes of DKT from Gujarat and Tamil Nadu.[6,7] There is no published data on outcomes of deceased donor organ transplantation from Maharashtra, a western Indian state.

Objective

The objective of this study was to evaluate outcomes of DKT done during five years between April 2012 to July 2017.

MATERIALS AND METHODS

In this retrospective study, medical records of all patients who received DKT from April 2012 to July 2017 were examined. The data was analysed for demographic profile of recipients and donors, comorbidities in recipients, cause of kidney disease in recipients, waiting period on dialysis, delayed graft function, episodes of rejections, induction agents used, maintenance immunosuppressants, infection episodes, patient and graft survival and causes of death.

All patients received deceased donor kidney allotted by Zonal Transplant Coordination Committee, Mumbai as per the waiting list prepared based on points for various parameters including dialysis vintage, vascular access failure, previous graft loss and patient age.[2] All the transplants were ABO compatible. CDC cross-match was negative in all transplants. HLA tissue matching, Luminex crossmatch and donor specific antibodies were not performed in any case. HTK solution was used and DJ stent was placed in all patients. All patients received heparin free haemodialysis just prior to transplant surgery.

Induction immunosuppression with two to three doses of anti-thymocyte globulin (1.5 mg/kg per dose) was given in all patients. Maintenance immunosuppression regimen included prednisolone, mycophenolate mofetil (MMF) and tacrolimus. Prednisolone was tapered to 5 mg/day over three months whereas MMF was continued at 1 gm twice a day and tacrolimus dose adjusted to keep the serum level at 6-7 ng/ml. All patients received cotrimoxazole and valganciclovir prophylaxis against pneumocystis jirovecii and cytomegalovirus (CMV) respectively.

Delayed graft function (DGF) was defined as need for dialytic support in the postoperative period and primary nonfunction graft (PNF) as one that never functioned.

Approval from the institutional ethics committee was taken.

Statistical Analysis

Continuous variables are presented as mean and standard deviation. Numbers and percentages are given for the categorical variables. Kaplan–Meier survival curve was used for survival analysis.

RESULTS

Recipient Characteristics

A total of 21 deceased donor kidney transplants (male 52.4%; female 47.6%) were performed during the study period. The baseline characteristics of the recipients are given in table 1.

Characteristics	Results
Age; mean (+ SD) in years	45.47 (±11)
Gender n (%)	
Male	11 (52.4)
Female	10 (47.6)
Cause of Renal Failure n (%)	
Chronic glomerulonephritis	03 (14.3)
Obstructive uropathy	03 (14.3)
Diabetic nephropathy	01 (04.8)
Lupus nephritis	01 (04.8)
Unknown	13 (61.9)
Comorbidities n (%)	
Diabetes	02 (09.5%)
Hypertension	17 (81%)
Ischemic heart disease	03 (14%)
Past history of tuberculosis (pulmonary/extra-pulmonary)	04 (19.1%)
Hepatitis C	03 (14%)
Hepatitis B	01 (04.8%)
Average duration of dialysis prior to transplant mean (±SD)	6.33 (±1.54)
years (range in years)	(2.94 – 10.16)

Table 1. Recipient Baseline Characteristics

One 58-year-old received a dual kidney transplant. In one patient tacrolimus was replaced with cyclosporine due to neurotoxicity.

Donor Characteristics

The mean age of donors was 47.8 years. Other baseline characteristics of donors are given in table 2. Eight donors (38.1%) were ECDs. The commonest causes of brain death in donors were head injury due to road traffic accidents and cerebrovascular accidents.

Characteristics	Results
Age; mean + SD in years	47.8+13.5
Age Group of Donors n (%)	
<50 years	13 (61.9)
50-59 years	05 (23.8)
>60 years	03 (14.3)
Gender n (%)	
Male	12 (57.1)
Female	09 (42.9)
Extended Criteria Donors **n (%)**	08 (38.1)

Table 2. Donor Baseline Characteristics

Post-transplant Outcomes

Two patients (09.5%) developed biopsy proven acute cellular rejection both responded to methylprednisolone

pulses. Delayed graft function, defined as requirement of dialysis post-transplant, occurred in three (14.28%) patients

One patient developed recurrent focal segmental glomerular sclerosis (FSGS), two months post-transplant which was treated with plasma exchange. The patient responded well to treatment with plasma exchange. His serum creatinine after treatment was 1.2 mg/dl and the urine protein excretion was between 400-800 mg/day. Now he is doing well after 50 months after transplant, with a serum creatinine of 1.3 mgs% and a urine protein excretion of 600 to 800 mgs/day. He also had lymphocele post-transplant requiring marsupialization and is on treatment with hepatitis B.

Patient survival at one, three and five years were 90.5%, 84.5% and 84.5% respectively. Four (19.04%) grafts were lost during the study period, three grafts were lost because of death of the patients (two at three months and one at 22 months post-transplant) and only one other graft was lost at 43 months with patient returning to dialysis. The graft survival curve can't be plotted as there was only one case of graft failure with return to dialysis at 43 months.

Outcome	Results
Patient Survival Rate	
One year	95%
Three years	84.5%
Five years	84.5%

Table 3. Patient Survival Rates

Three patients (14.2%) died during the study period; two because of cardiovascular disease and other two due to sepsis (figure 4). One patient returned to haemodialysis because of graft dysfunction nine months post-transplant due to sepsis following road traffic accident.

Seven (33.3%) patients developed bacterial chest infections. One of them had atypical mycobacterial infection and cryptococcosis of lung whereas one developed acute respiratory distress syndrome (ARDS) requiring hospitalization and intensive care. Post-transplant urinary tract infections occurred in five (23.8%) patients, out of which one had recurrent episodes because of significant post void bladder residue due to autonomic neuropathy. One (04.8%) patient developed chickenpox over trigeminal nerve distribution and one (04.8%) had cytomegalovirus (CMV) infection (table 4).

Six (28.6%) recipients developed new onset diabetes after transplant (NODAT). Significant drug related complications, other than NODAT, requiring stopping or holding the drug developed in five (23.8%) patients. Three (14.3%) patients developed leukopenia needing permanent discontinuation of MMF in one and temporarily in two. One (04.8%) patient needed replacement of tacrolimus with cyclosporine due to neurotoxicity. Ribavirin induced haemolysis (04.8%) was observed in one patient who received it for HCV infection needing temporary discontinuation with reintroduction at lower dose (table 4).

Complication	Results n (%)
Death	03 (14.3%)
Causes of death	
• Cardiovascular cause	01 (33.3%)
• Sepsis	02 (66.7%)
Infections:	
• Bacterial chest infections	07 (33.3%)
• Post-transplant urinary tract infection	05 (23.8%)
• Intraabdominal pus collection	01 (04.8%)
• Chicken pox	01 (04.8%)
• CMV infection	01 (04.8%)
Other complications	
New onset diabetes after transplant	06 (28.6%)
Leucopenia	03 (14.3%)
Hypotension requiring inotropic support	02 (09.6%)
Lymphocele requiring surgical intervention	01 (04.8%)
Recurrent FSGS	01 (04.8%)
Cyclosporin induced neurotoxicity	01 (04.8%)
Ribavirin induced haemolysis	01 (04.8%)

Table 4. Complications During the Study Period

DISCUSSION

Although presently only 5% of the total renal transplants are DKT,[3] the trend is fast improving particularly in the western and southern states of India.[4]

The gender disparity in live donor renal transplants which is highly biased against women is lacking in the present study for obvious reasons. There were 52.38% (11/21) and 57.1% (12/21) male recipients and donors respectively. Whereas in the live donor program from this same hospital there were 83.6% and 14% male recipients and donors respectively (unpublished data). Similar observations were made in other studies.[7,8]

In the current study, the average duration of dialysis before transplant was 6.33 (+1.54) years as opposed to two years in another study from India.[6] A longer waiting period on dialysis is possibly because of better survival rates on MHD in patients waiting for a kidney rather than lesser availability of donors. The long waiting time on dialysis has a direct effect on the general health. It is clearly seen that patients with longer dialysis vintage have poorer general health. This translates into negative impact on the transplant outcome, particularly in the immediate and early post-transplant period.[9] In the current study 2 patients died in the first 6 months of transplant surgery due infection and sepsis.

There was no PNF graft in the current study. This is in contrast with another study where primary non-functioning graft rate was reported as 15% from a large volume centre.[7] Three patients out of 21 (14.2%) had DGF. Two of these are doing well. One died after 3 months of transplant because of sepsis. In a study from south, the incidence of DGF was 48.5%. There was a higher incidence of graft loss in patients with DGF in that study.[7] High mortality in patients with DGF was also reported by Patel et al.[10]

The incidence and prevalence of chronic kidney disease is rising in India, attributed mainly to rise in diabetic nephropathy.[11] In the current study, after the unknown causes, chronic glomerulonephritis and obstructive uropathy were more frequent causes for ESKD. Diabetic nephropathy accounted for only 4.8% (1/21) of the patients in the current

study. This is because the average waiting time on dialysis is 6.33 (+1.54) years, which is too long for this population of patients with their comorbidities to remain fit for kidney transplant surgery. In a recently published study from Kerala, South India, the mean survival in patients with diabetic nephropathy in a tertiary care hospital was 35.93 months and that in the non-diabetic renal disease was 47.46 months.[12]

Induction therapy helps prevention of acute rejection particularly in the first year.[13] Variations exist in the protocols of using induction therapy in India. Two major induction agents used include anti-thymocyte globulin and basiliximab. All patients in current study received two to three doses of anti-thymocyte globulin (1.5 mg/kg per dose) as compared single dose in the other studies.[6,7] These two studies using single dose of induction with anti-thymocyte globulin have reported an acute rejection rate of 21.8% and 20.7%.[6,7] Biopsy proven acute cellular rejection rate in current study was 9.5%. There was no case of antibody mediated rejection. It must however be noted that the sample size in current study was much smaller then both these studies.

The survival of patients receiving transplant is lower compared to age-matched controls in the general population.[14] The patient survival rate at the end of the first year was 90.5%, at the end of second year it was 84.5% and at the end of 5 years it remains 84.5%. In study from India, the one-year patient survival rate was 80.3%[7] while another reported it to be 81.7%.[6] One-year patient survival in current study was numerically better as compared to these studies, but statistical difference is not known as the number of patients is small in the current study.

Infection is one of the major challenges in the post-operative period in patients with kidney transplant in developing nations. The contributing factors for increased risk of infections include low socio-economic status and environmental conditions.[6] In current study, bacterial chest infections were the most common, being observed in 33.3% patients followed by post-operative urinary tract infection observed in 23.8% patients. One of the patients with chest infections also developed atypical mycobacterial infection and cryptococcosis of lung. Only one had CMV disease.

The overall mortality rate in the current study was 19.1% at 3 and 5 years. The common causes of mortality in post-transplant patients include infection, cardiovascular disease, cerebrovascular disease and graft failure.[14] As reported in a study from India,[6] in the current study too, infections (66.7%) and cardiovascular diseases (33.3%) were the most common causes of mortality post-transplantation. Sepsis has also been reported to be a common cause of death in another study from India.[7]

Limitations of the Study

The current study has some limitations. As the average follow up period was short, the five-year survival reported may not be representative. Results of current study should be interpreted with considerations of single centre data, small sample size and short duration of follow up period.

CONCLUSION

The results of current study suggest that DKT provides acceptable outcomes even though the waiting period on dialysis was too long, only CDC lymphocyte crossmatch was done, HLA tissue typing was skipped and there were 38% extended criteria donors. With time, all these issues will be sorted out and the outcomes are expected to better in the future.

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