

Outcome of cadaveric renal transplantation, single centre experience: A retrospective and prospective clinical study

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Abstract

Background: Cadaveric renal transplant is a robust in Tamilnadu, giving a new lease of life to so many patients with End stage renal disease. Aim: This is a study done in a tertiary care hospital in South India to find out the recipient and donor characteristics, graft and recipient survival, perioperative complications and infection rates outcome of cadaveric renal transplant program. Materials and method: This was a prospective and a partly retrospective study conducted from October 2008 to March 2014. **Conclusion:** The survival rates for both patient and graft of deceased donor transplantation is equal to that of live related renal transplantation. Our deceased donor program demonstrates that it can be implemented successfully as long as the framework of the program maintains transparency and adheres to established protocols.

Key Word: cadaveric renal transplantation.

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INTRODUCTION

The biggest medical breakthroughs of this century are transplantation of human organs. The escalating End stage Renal Disease population and the lack of suitable donors – this discrepancy is well known. The first deceased donor renal transplantation in our hospital was performed in the year 1996 with 73 deceased donor transplantations performed thereafter. Though deceased donor transplantation was started in the year 1996, it started gathering momentum only after the year 2008, when a

doctor couple donated their brain-dead son's organ, which gained widespread public attention.

India has a high incidence and prevalence of CKD and ESRD¹. The rate of deceased donors per million in India is far behind the world average rate. When compared with other countries like United States, Portugal and Spain the renal transplantation rate in India with a population of about 1.3 billion is only 3.2 per million populations. The major causes of End Stage Renal Disease are Diabetes and Hypertension which is on the increase. The age-adjusted incidence of end stage renal disease is estimated to be 232 per million populations. The only hope for patients with ESRD is renal transplantation², as the dialysis centres are limited to certain regions especially they are concentrated in the urban cities and is also expensive in the long run. The importance of this scenario is exemplified by this. The only way to combat the commercial organ transplantation is to increase the deceased donor transplantation³. It also reduces the burden on the live related renal transplantation. Until a decade ago there was a lack of knowledge among the general public

about deceased organ donation. But the crucial role played by the non - government organization and the media in

India⁴, the government implemented the deceased donor programme in the state of Tamilnadu successfully.

AIMS

1. To analyse the various donor and recipient characteristics.
2. To analyse the post transplant infections and post operative complications
3. To analyse the infection rates and acute rejection rates with the use of induction immunosuppression.
4. To analyse the patient survival rates.
5. To analyse the graft survival rates.

MATERIALS AND METHODS

OBSERVATION AND RESULTS

This was a prospective and a partly retrospective study conducted from October 2008 to March 2014.

INCLUSION CRITERIA

All patients who underwent deceased donor renal transplantation in our centre were included in the study.

EXCLUSION CRITERIA

All patients who underwent live renal transplantations were excluded from the study.

STATISTICAL METHODS

The various donor and recipient characteristics, cold ischemic time (CIT), tacrolimus levels, post transplant infections were analysed using multivariable Cox regression model, Pearson chi square test, Fisher's exact test.

Kaplan-Meier analysis to evaluate survival rates of patient and graft at 1 year and 4 years.

Table 1: Total no of Deceased donor transplantations

Gender	Frequency	Percent
Male	54	74.0
Female	19	26.0
Total	73	100.0

Table 2: Blood group wise distribution

BLOOD GROUP	Frequency	Percent
A	12	16.4
B	25	34.2
AB	7	9.6
O	29	39.7
Total	73	100.0

Table 3: Descriptive statistics

Variable	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	73	18	57	34.03	7.893
Cr- 1wk (mg/dl)	67	.80	13.10	2.5269	2.34150
Cr-1Mon	59	.80	5.60	1.3034	.71026
Cr- 6Mon	41	.80	1.70	1.1415	.20122
on HD-months	71	1	60	20.14	13.011
Recent Cr (mg/dl)	40	.7	2.7	1.453	.4261
Tacro Level (ng/ml)	64	2	18	6.74	4.056
Age of donor (years)	73	12	68	33.51	13.299
CIT (hours)	72	3	15	8.01	2.737
No of days alive	73	0	1891	733.14	593.439

The mean duration of Haemodialysis prior to transplant was 20.14 (\pm 13) months. The overall mean age of the recipient was 34 (\pm 7.8) years. The overall mean age of the donor was 33.51 (\pm 13.3) years. HTK (Custodiol) was the organ perfusion solution used in all patients. The mean cold ischemic time was 8.01 (\pm 2.73) hours. Total recipients who had received induction immunosuppression were 13 patients. Anti-Thymocyte Globulin, rabbit origin (rATG) was used in 6 patients. Interleukin-2 receptor antagonists (Basiliximab) were used in 7 patients. Significant intra-operative events encountered in 10 patients such as

- Bleeding: 2
- Mottling: 1
- Hypotension: 4
- Impending graft rupture: 1
- Accessory artery to External iliac artery: 2

Significant post-operative complications were encountered in 30 patients

- Sepsis: 7
- Delayed graft function : 6
- Graft nephrectomy : 4
- Persistent drain (lymphocele) : 9
- Pancreatitis : 3
- Right lower limb ischemia : 1

INFECTIONS DURING FOLLOW UP

- Pneumonitis : 7
- Sepsis : 10
- Recurrent UTI and BK virus : 1
- HCV Related DCLD : 1
- Mycobacterial tuberculosis – 3 (Joint TB in 1, Pulmonary in 2)

Table 4: Gender of donor

		Frequency	Percent
Valid	Male	57	78.1
	Female	16	21.9
Total		73	100.0

PATIENT SURVIVAL USING KAPLAN-MEIER

Number of Cases: 73 Censored: 28 (38.36%) Events: 45

Patient survival at the end of 1 year is 89.33 %

Patient survival at the end of 3 years is 50.40 %

Table 5:

	Survival Time	Standard Error	95 % Confidence Interval
Mean	1079	71	(939, 1219)
Median	1168	144	(885, 1451)

GRAFT SURVIVAL (CENSORED FOR DEATH)

Number of Cases: 73 Censored: 14 (19.18%) Events: 59

Table 6:

	Survival Time	Standard Error	95 % Confidence Interval
Mean	869	73	(725,1013)
Median	752	206	(348,1156)

Total number of deceased donor transplantations was 73 up to March 2014. Though the deceased donor programme began in the year 1996, it started gathering momentum only after 2008, when a doctor couple donated their son's organs who sustained RTA which drew widespread public attention. In Tamil Nadu the total number of deceased donor transplantations was 425, and the total number of organs shared was 2315 including 825 kidneys⁵. The number of male recipients was 74 % (n=54) outnumbering female recipients which the usual scenario even in live renal transplantation. The number of female recipients was only 26 % (n=19). Our institution tops the list next by contributing to 14 donors which comes to 19.1 %. The other private hospital from the city and the state contributed to the rest of organs donations.

BLOOD GROUP WISE DISTRIBUTION

As is the prevalence of blood group so is the transplantation. O blood group being more common tops the list of transplantations, it accounts for 39.7 % (n=29). B blood group tops the list next with 34.2 % (n=25) and A has 16.4 % (n=12) and AB blood group is the least prevalent blood group accounting for only 9.6 % (n=7) of the total deceased donor transplantation.

CAUSES OF BRAIN DEATH

Road Traffic Accidents (RTA) tops the list accounting for the majority of donations. As is already evident from the gender of the donors the majority are males who sustain RTA without wearing an helmet. The next most common cause of death is fall from height, who are usually construction site labourers without adequate safety

precautions. The other causes of brain death are berry aneurysmal bleed, Sub-arachnoid hemorrhage among hypertensives and alcoholics and traumatic asphyxia in a factory worker due to fall of heavy object over his chest.

NATIVE KIDNEY DISEASE

The prevalence of Native kidney disease among recipients is as follows, the cause is not known in the majority of patients, which is the usual scenario as they are asymptomatic in the earlier stages of the disease; they are on poor follow up after detection of renal failure and refusal for renal biopsy in the earlier stages of the disease. They usually present with overt uremic symptoms when they have small contracted kidneys and renal biopsy could not be performed. Hence the cause is presumed to be CGN/CIN in 37 (50.7 %) patients.

1. Biopsy proven Chronic Glomerular Disease was demonstrated in only 27 (37 %) patients.
2. Alport's syndrome was the cause of renal failure in 2 (2.7 %) patients.
3. Autosomal Dominant Polycystic kidney disease (ADPKD) was the cause of renal failure in 2 (2.7 %) patients,
4. Focal Segmental Glomerulo sclerosis was the cause in another 3(4.1 %) patients and
5. Systemic Lupus Erythematosus was found in 1 patient (1.4 %).

WAITING PERIOD PRIOR TO TRANSPLANT

The mean duration of Haemodialysis prior to transplant was 20.14 (\pm 13) months. The median waiting period for transplantation is 1.5 years in our centre. The number of patients on each blood group is 15 except for AB blood group and the number deceased donor transplants per year are 10 on an average. Hence there is a long waiting period prior to transplant.

MEAN AGE OF THE DONOR AND RECIPIENT

The overall mean of the donor and recipient was 34 (\pm 7.8) years and 33.51 (\pm 13.3) years, since most of the donors were male who sustain RTA, they are relatively young. The recipients also have to come for follow up every month and have withstand dialysis for at least two years, the average waiting period. Hence the recipients are also young.

ORGAN PERFUSION AND PRESERVATION

HTK (Histidine-Trptophan-Alpha Ketoglutarate) – CUSTODIOL⁶ was used in all the deceased donor transplantations. The sterile three bag technique is used for packing and transportation is done in sterile ice.

COLD-ISCHEMIC TIMES

The mean Cold Ischemic times was 8.01 (\pm 2.73) hours. It varied between a minimum of 3 hours when the organ harvest takes place in our centre and is up to 15 hours when the organ harvest takes place in other centres.

Delayed graft function (DGF) and Slow graft function (SGF) was observed whenever the cold ischemic time is more than 10 hours. Out of the 28 patients who had DGF and SGF, nearly twenty of them had cold ischemic time of more than 8 hours.

INDUCTION AGENTS

Induction agents became part of the protocol after 2012 and it is being given totally free of cost in government hospitals. Only 13 patients had received induction agents out of 73 deceased donor transplantations. Anti-Thymocyte Globulin – rabbit origin (rATG) was used in 6(8.21 %) patients. A single dose of 1.5 mg/kg was given as intravenous infusion in the preoperative and intraoperative period. T. Valganciclovir 450 mg twice daily is given for three months for CytomegaloVirus prophylaxis for all patients who had received ATG as induction agent. Among the rATG group⁷, 3 patients died, pneumonitis was the cause of death in all the three patients. One patient had knee joint tuberculosis and tuberculous laryngitis. Interleukin-2 receptor blockers (Basiliximab) was used in 7(9.58 %) patients. Two doses of 20 mg each is given at 4 days interval. Among the Basiliximab group one patient died due to pneumonitis of tuberculosis..

Graft Biopsy was performed in 14 patients, Acute cellular rejections were seen in 7 (9.58 %) patients. Out of 7, 4 was early acute rejections and 3 was late acute rejections. All of them responded to steroids. Acute Antibody Mediated rejections was seen in 2 (2.74 %), both improved with plamapheresis. Acute Tubular Necrosis was seen in 6 (8.21 %) patients.

FOLLOW-UP

The mean follow – up period 4 years. The recent mean serum creatinine is 1.45 mg/dl. Post - Transplant Diabetes (PTDM) was seen in 10 (13.69 %) patients. Post transplant Erythrocytosis was observed in 8 (10.96 %) patients. The mean tacrolimus was 6.75 (\pm 4.05) ng/ml as measured by Chemiluminiscent Microparticle Immunoassay.

VIRAL SEROLOGY

One patient was HCV positive prior to transplant. One patient was HBsAg positive prior to transplant , he died due to pneumonitis. One patient who was HCV negative prior to transplant became HCV positive, had Decompensated liver disease and hepatic encephalopathy and died.

PATIENT STATUS

Out of 73 renal transplantations 28(38.4 %) patients died. Patient survival at the end of 1 year is 89.33 % and at the end of 4 years is 56,40 %.

GRAFT SURVIVAL (Censored for death)

Graft survival at the end of 1 year is 73 % and at the end of 3 years is 44%. The patient and graft survival rates are very much comparable to that of live related renal transplantation.

CONCLUSIONS

The survival rates for both patient and graft of deceased donor transplantation is equal to that of live related renal transplantation. Only way to combat the illicit organ trading (commercial renal transplantation) is deceased donor transplantation. Cadaver organs should be considered as nation's resource and organs wasted should be treated as lives lost. Our deceased donor program demonstrates that it can be implemented successfully as long as the framework of the program maintains transparency and adheres to established protocols. Hence deceased donor transplantation is the need of the hour, which can be promoted by positive public attitude, identification of early brain death and certification, getting prompt consent for organ donation and adequate hospital infrastructure are essential prerequisites for successful organ transplantation. The state of Tamil Nadu would definitely be a good role model in this regard.

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