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PREDICTORS OF EARLY AND DELAYED GRAFT FUNCTION IN LIVE AND CADAVERIC RENAL TRANSPLANTATION

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Abstract

Background: Kidney transplantation gives the best quality of life to chronic kidney disease patients and also increases longevity.
Aim: Analysis of factors responsible for the early and delayed graft functioning in live and cadaver renal transplants
Patients and Methods: It was a retrospective observational study. Donor and recipient age, sex, BMI, comorbid illness, and functioning status of the donor kidney, duration and severity of chronic kidney disease and associated bladder disorders were collected. Operative factors like perfusion time, cold ischemia time, blood pressure fall, need for blood transfusion, vasopressor support was recorded. Patients were divided into two groups based on early versus delayed graft function.
Results: 27 cases of Live donor renal transplant and 23 cadaver transplants were included. The average age in live donor and cadaveric transplants was 43.5 ±7.6 years and 38.3 ±10.5 years, respectively. 24 Live Transplant Recipients had Early Graft function (89%). Seven Cadaveric Transplant Recipients had Early Graft function (31%) and 16 of them had Delayed Graft Function (69%). HLA Mismatch, Perioperative Hypotension and BMI of recipient had statistically significant relationship to Early Graft Function with p values of 0.02, 0.004 and 0.007, respectively. With p-value of 0.021 and of 0.046, respectively, perioperative hypotension and cold ischemic time in Cadaveric renal transplantation had statistically significant relationship to Early Graft Function.
Conclusion: Live donor transplants have better early graft function. HLA Mismatch, Perioperative Hypotension, BMI of recipient and cold ischemic time in Cadaveric renal transplantation are the predictors of early graft function.

Keywords: Cadaveric, Early Graft Function, Kidney transplantation

Introduction:

Chronic Kidney disease (CKD) is one of the major cause of mortality and morbidity in the world today. Diabetes mellitus, Hypertension and Glomerulonephritis are the leading causes of chronic kidney disease [1]. The Kidney Disease Outcomes Quality Initiative (KDOQI) and the international guideline group of Kidney Disease Improving Global Outcome (KDIGO) have defined chronic kidney disease as either kidney damage or decreased Glomerular filtration rate (GFR) of less than 60ml/min/1.73m2 for at least 3 months [2].

Different options for Renal Replacement Therapy (RRT) include peritoneal dialysis (PD), intermittent haemodialysis (IHD), sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD) and continuous renal replacement therapy (CRRT) and Renal transplantation[3]. Out of these, kidney transplantation

gives the best quality of life and probably also increases longevity [4].

There are two main types of renal transplantation; live renal transplantation and cadaver renal transplantation. in the past 45 years, the live donor kidney transplantation program in India has evolved. It is currently the second largest program in numbers after the USA [5]. The prevalence of end-stage renal disease which requires transplantation in India is estimated to be between 151 and 232 per million population[6]. Approximately 220,000 people require kidney transplantation in India. Against this, currently, approximately 7500 kidney transplantations are performed at 250 kidney transplant centres in India. Of these, 90% come from living donors and 10% from deceased donors.

Transplantation is an example of a multi-disciplinary team approach involving not only urologists and nephrologists but also anaesthetists and pathologists working in concert to produce the best results for the patient[7]. Despite being done with good surgical expertise and proper nephrological management, some cases of renal transplant recipients do not achieve the long term expected graft function. One of the factors predicting the long term graft functioning is the evaluation of early graft function one week after transplant[8].

In our study, we analyzed various factors responsible for the early and delayed graft functioning of both live and cadaver renal transplants.

Patients And Methods:

It was a retrospective observational study conducted in our institute at the department of urology for 2 years. All the patients undergoing renal transplantation during the study period were included in the study, except those patients who had undergone previously failed transplantation. The study was conducted after taking approval from the institutional ethical committee.

The data collected included Donor and Recipient age, sex, BMI, comorbid illness, blood group match, the functioning status of the donor kidney (renogram), duration and severity of chronic kidney disease, and associated bladder(cystogram) disorders. Various operative factors like perfusion time, cold ischemia time, type of perfusion solution, perfusion before versus after bench dissection, and anastomosis time were also noted. Some inadvertent factors like blood pressure fall, need for blood transfusion, and vasopressor support was recorded. In this study, we analyzed recipient factors which can cause delayed graft functioning and mainly the factors responsible from the urological standpoint were studied. Then the serum creatinine at the end of the first-week post-transplant and/or the need for dialysis were all recorded.

Patients were divided into two groups (Group A & B) based on early versus delayed graft function.

The above data collected was analyzed. Chi-squared test was used to test the strength of association and a p-value of <0.05 was considered statistically significant. Statistical analysis was done using SPSS version 26.

RESULTS:

Fifty patients underwent renal transplantation which included 27 cases of Live related renal transplants and 23 cadaver transplant (Deceased Brain donor) cases. The demographic profile of the patients is shown in Table I.

Tables 1:Demographic Profile Of Donor And Receipt :

		Live Recipients	Live Donors	Cadaver Recipients	Cadaver Donors
Age Distribution (Years)	10-20	4	0	1	0
	21-30	14	3	4	7
	31-40	7	5	9	2
	41-50	2	15	4	11
	51-60	0	4	5	3
	Total	27	27	23	23
Gender	Male	20	5	15	18
	Female	7	22	8	5
	Total	27	27	23	23

The average age of the live transplant donor was 43.5 years with a standard deviation (SD) of 7.6 years. The average age of cadaveric transplant recipients was 38.3 years with an SD of 10.5 years. Twenty four Live Transplant Recipients had Early Graft function (89%) and 3 of them had Delayed Graft Function (11%) Figure 1.

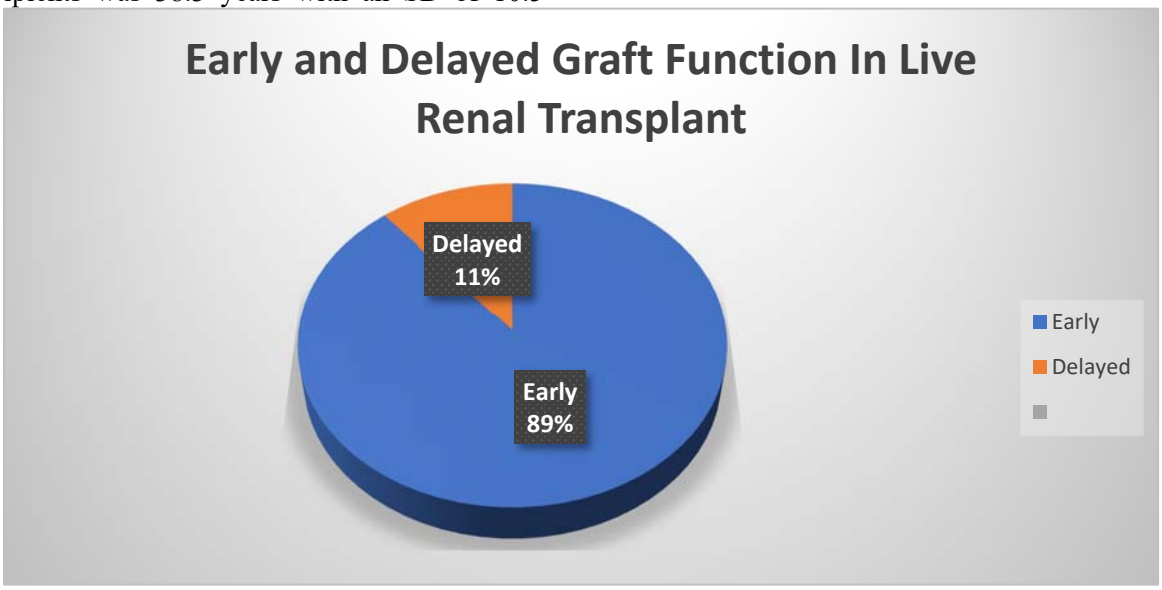

Figure 1: Early and Delayed Graft Function in Live Renal Transplant.

Seven Cadaveric Transplant Recipients had Early Graft function (31%) and 16 of them had Delayed Graft Function (69%). Figure 2

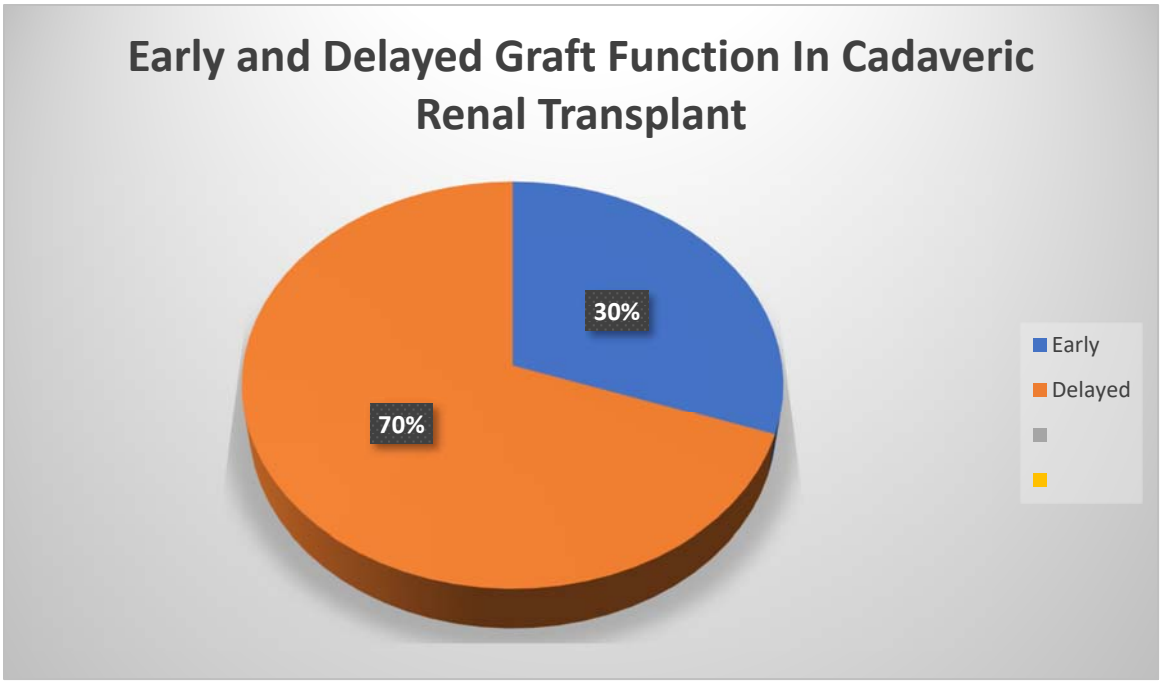

Figure 2: Early and Delayed Graft Function In Cadaveric Renal Transplant

Live recipient age, recipient gender and live donor age had no statistically significant relationship to Early Graft Function (EGF) with p values of 0.81, 0.75 and 0.71, respectively Table II.

Table II: Univariate Analysis Of Age And Gender Of Recipient, Donor Age And Early Graft Function In Live Related Renal Transplantation

		Early Graft Function	Delayed Graft function	Total	
Recipient age Categories (Years)	10-20	4	0	4	Chi Sq.0.964 p- value- 0.810
	21-30	12	2	14	
	31-40	6	1	7	
	41-50	2	0	2	
Total		24	3	27	
Donor Age categories (Years)	21-30	3	0	3	Chi Sq.- 1.35 p- value- 0.717
	31-40	4	1	5	
	41-50	13	2	15	
	51-60	4	0	4	
Total		24	3	27	
Gender of Recipient	Male	18	2	20	Chi Sq.0.096 p- value- 0.756
	Female	6	1	7	
Total		24	3	27	

HLA Mismatch, Perioperative Hypotension and BMI of the recipient had a statistically significant relationship to Early Graft Function with p values of 0.02, 0.004 and 0.007, respectively. With a p-value of 0.26, the duration of the cold ischemic time during the Live Renal Transplantation had no statistically significant relationship to the Early Graft Function Table III.

Table III: Univariate Analysis of HLA mismatch ,hypotension ,cold ischemia time, BMI of recipient and Early Graft function in Live related Renal Transplantation

HLA Mismatch	2	8	0	8	Chi Sq.- 9.6 p- value- 0.02
	3	12	2	14	
	4	0	1	1	
	6	4	0	4	
Total		24	3	27	
Hypotension	Yes	0	1	1	Chi Sq.- 8.3 p- value- 0.004
	No	24	2	26	
Total		24	3	27	
Cold ischemia time	< 30min	16	1	17	Chi Sq.- 1.27 p value-0.26
	>30 min	8	2	10	
Total		24	3	27	
BMI of recipient	Normal	22	1	23	Chi. Sq.- 7.19 p value-0.007
	Overweight	2	2	4	
Total		24	3	27	

Most of the biopsies done in recipients (66%) with delayed graft function were found to have Acute tubular necrosis Table IV.

Table IV: Renal Biopsy in Live recipients with Delayed Graft Function

Renal Biopsy	Number	Percent (%)
Acute tubular necrosis	2	66.6%
Antibody Mediated Rejection	1	33.3%
Total	3	100

The spot-PCR was measured among the 23 cadaveric donors. The mean was found to be 0.61 with a Standard Deviation of 0.34. With a p-value of 0.105, Spot PCR of Donor in Cadaveric renal transplantation had no statistically significant relationship to Early Graft Function. With a p-value of 0.046, Cold ischemic time in Cadaveric renal transplantation had a statistically significant relationship to Early Graft Function. With a p-value of 0.068, the BMI of the recipients in Cadaveric renal transplantation had no statistically significant relationship to the Early Graft Function Table V.

Table V: Uni-variate analysis between Cold ischemic time ,BMI, Spot PCR, Hypotension and Early Graft function in Cadaveric renal transplants.

		Early Graft Function		Total	
		Yes	No		
Cold Ischemic Time in Cadaveric Transplant	Less than 480 Mins	5	4	9	Chi Sq.- 5.75 p value-0.046
	480-600 mins	2	5	7	
	More than 600 mins	0	7	7	
Total		7	16	23	
BMI Categories	Normal	7	8	15	Chi Sq.- 5.367 p value-0.068
	Overweight	0	6	6	
	Obese	0	2	2	
Total		7	16	23	
Spot PCR	Less than 0.5	5	7	12	Chi Sq.- 4.5 p value-0.105
	0.5-0.99	0	7	7	
	More than 1	2	2	4	
Total		7	16	23	
Hypotension	Yes	0	8	8	Chi Sq.- 5.367 p Value - 0.021
	No	7	8	15	
Total		7	16	23	

Higher age group category donors had a higher number of delayed graft functions i.e., donors older than 41 years of age resulted in DGF in 78% of recipients. But the age of the donors in Cadaveric renal transplantation was not found to be statistically significant probably because of the lesser sample size.

Cause of Death of Donors, Age of recipient and Gender of the Recipient and Donor in Cadaveric renal transplantation had no statistically significant relationship to Early Graft Function with P values of 0.64,0.80,0.172 and 0.59, respectively.

With a p-value of 0.021, Perioperative Hypotension in the early postoperative period in Cadaveric renal transplantation had a statistically significant relationship to Early Graft Function. Table VI.

Table VI: Uni-variate analysis between Age and Gender of recipient and donor, cause of death and Early Graft function in Cadaveric renal transplant.

		Early Graft Function		Total	
		Yes	No		
Age of the Recipient	10-20	0	1	1	Chi Sq.- 1.641 p Value - 0.80
	21-30	1	3	4	
	31-40	4	5	9	
	41-50	1	3	4	
	51-60	1	4	5	
Total		7	16	23	
Age of Donor	21-30	3	4	7	Chi Sq.- 2.236 p value-0.525
	31-40	1	1	2	
	41-50	3	8	11	
	51-60	0	3	3	
Total		7	16	23	
Gender of Recipient	Male	6	9	15	Chi Sq.- 1.8 P value- 0.172
	Female	1	7	8	
Total		7	16	23	
Gender of Donor	Male	5	3	8	Chi Sq.- 0.276 P value- 0.59
	Female	2	13	15	
Total		7	16	23	
Cause of Death	RTA	6	11	16	Chi Sq.- 0.884 p Value - 0.64
	IC bleed	1	4	5	
	Electric Burn	0	1	1	
Total		7	16	23	

Discussion:

A successful long-term outcome for a new kidney transplant recipient depends on the early perioperative management and course after surgery. Important factors predicting long-term outcomes include the occurrence of delayed graft function (DGF); episodes of acute rejection; early surgical complications, such as urinary obstruction, urine leak, or vascular complications; and sepsis.

Early complications of renal transplantation may be mechanical/surgical or medical. Early medical problems are more common than post-transplant surgical problems The most common early post-transplant medical problem is DGF[9]

We analyzed demographic features of renal transplant recipients and donors, causes of acute graft dysfunction, and factors influencing Early

graft function in patients undergoing Cadaveric and Live renal transplantation at our institute.

This study included a total of 27 cases of Live related Renal transplants and 23 cadaver transplant (Deceased Brain donor) cases.

The mean age of the live transplant recipient was 29.2 years with an SD of 8.11 years and the average age of the cadaver transplant recipient was 38.3 years with an SD of 10.5 years. There were more male patients in the living donor group 74% (20 recipients), whereas in the cadaver group 65% (15 recipients) were male.

Most of the Live donors in our study were in the age group 41-50 years (55.6%) followed by the age group 31-40 years. The mean age of Live donors in our study was 43.5 years with a standard deviation of 7.6 years which was almost similar to the study done by E Nemati et al[10](41 years) and the study by Rajani Hada et al[11] (43.04 years) whereas it was much lower than the studies of VB kute et [al12which] was 58.3 years.

The mean age of Deceased Brain donors in our study was 38.3 years which was almost similar to the study done by Gopalakrishnan et al[13](32 years), whereas it's much lower than the studies of YK Swami et [al14which] was 46 years and VB kute et al[12] which was 45.9 years. The less mean donor age in our study might be due to the younger age group of people involved in road traffic accidents.

In our study, among Live donors, Female donors outnumbered male donors. 81.5 % of donors were females and 18.5 % of donors were males with an M: F ratio of 1: 4. The gender distribution among the Live Donors is similar to the study by Rajani Hada et al [11], where 79% of donors were female and 21% of donors were male.

Among Deceased brain donors in our study, 78.26% were males and 21.14% of donors were females with an M: F ratio of 3.6:1 which was higher than in the study done by H.V. Patel [15] et al which was 2.18:1, Yazdani et al [16] which was 2.58: 1. It was less than the study of Gopalakrishnan et al[13] where the M: F ratio was 6:1. Road traffic accidents were the main cause of brain death in our study constituting 73.9 % of cases followed by intracranial bleeding which constitutes 21.7% of cases.

In our study, 88.9% of the Live renal transplant recipients had Early Graft Function while the remaining 11.1% had Delayed Graft Function. The incidence of DGF was slightly higher compared to the studies done by MR Mogula et al[17]and Robert R Redfield et al[18].30.4% among the Deceased Donor Renal transplant recipients had Early Graft function and 69.6% had Delayed Graft function. It was similar to a study done by Kunal Kapoor et al[19] where it was 65% and higher compared to a study by Y K Swami et al [14]where it was 34% and VB Kute et al[15] where it was 30%.

We did a Univariate Analysis of various Donor and Recipient characteristics with Delayed Graft Function. Among the Live Transplant HLA mismatch between Donor and Recipient, Perioperative Hypotension and BMI of the Recipient were found to have statistically significant relation with delayed Graft function whereas Age and Gender of the donor, Age and Gender of the recipient, ABO incompatibility, Cold ischemic time had no statistically significant relation with Delayed Graft function. Among the Deceased donor renal transplant, Cold Ischemic time and perioperative Hypotension were found to have a statistically significant relation with delayed Graft function whereas Gender of the donor, Age and Gender of the recipient, Cause of Death of the Donor, Spot PCR had no statistically significant relation with Delayed Graft function. Higher age group category donors had a higher number of delayed graft function i.e., Donors older than 41 years of age resulted in DGF in 78% of recipients. But Age of the donors in Cadaveric renal transplantation was not found to be statistically significant probably because of the lesser sample size. Similar results were found in the study by Martin Chaumont et al[20]

On biopsy in cases of delayed graft function, the most common finding was Acute tubular necrosis 66.6% among Live transplants and 81.25% among Deceased donor transplant recipients followed by rejection 33.3% in Live and 18.75% among Deceased donor Transplant recipients. Similarly, in the study by Evaldo Favi et al [21] the main cause of DGF was acute tubular necrosis (ATN) in 88% of cases, and acute rejection in 8% of cases. Similarly in a study by Y K Swami et al [14], ATN was observed in 50% of cases of DGF.

Conclusion: DGF in the immediate postoperative period necessitates the use of dialysis which adds a significant cost impact to patient management, also complicating post-transplant management as an outpatient. Thus,

achieving early graft function is of paramount importance. Avoiding Perioperative Hypotension, optimizing the BMI of the recipient, and Decreasing Cold ischemia time in Cadaveric transplant will improve the early graft function in Live transplants. Cold ischemia time can be significantly reduced with good coordination between organ retrieval and transplant teams. Every effort should be made to minimize the effect of these factors to optimize the Early Graft function and improve the overall outcome of Renal transplantation.

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Author 5 -Literature Review.
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Availability of Data and Material:
The corresponding author is prompt to supply datasets generated during and/or analyzed during the current study on wise request..

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