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Prevalence and factors leading to delayed graft function and slow graft function in living donor kidney transplantation at tertiary care hospital, Karachi.

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Abstract

Introduction: The level of function of a transplanted kidney in the immediate postoperative period is correlated with long-term graft. Delayed graft function (DGF) is associated with acute rejection, prolonged hospital stays, and healthcare costs, as well as increased rates of graft failure.

Objectives of study was to determine the frequency of DGF and Slow graft function (SGF) among living donor kidney transplants. Secondly, to compare frequency of factors responsible for slow and delayed graft function.

Subjects and methods: Descriptive study done at Department of Transplantation, Sindh Institute of Urology and Transplantation, from 22nd October 2019 to 23rd April 2020. All patients undergoing first living donor renal transplants of both genders with recipient age 18-50 years and had ESRD due to all causes were included. The data related to donor factors, recipient factors, and transplant factor were noted. The frequency of SGF and DGF was noted after early post-transplant period. The leading factors evaluated for the SGF & DGF were compared with IGF.

Results: The mean age of the donors was 32.15 ±8.68 years. Only 9 (5.7%) donors had >50 years age whereas female gender was reported as 65 (41.1%). BMI >30kg/m2 was found in only 2 (1.3%) recipients. The mean warm ischemia time was 1.01 ±1.36. None of the patient

had WIT of >30. IGF was found in 154 (97.50%) patients, SGF in 3 (1.9%) and DGF in 1 (0.6%) patient.

Conclusion: The frequency of DGF was found to be 0.6% and SGF 1.6% among living donor kidney transplants.

Keywords: Delayed graft function, slow graft function, living donor kidney transplants

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DOI:
Received 17 June 2024 and accepted 30 June 2024. PJKD 2024;8(2):11-17

Introduction

End stage kidney disease patients only option of a better life with kidney transplantation has seen significant improvement in outcomes over time.[1] Living donor kidney transplantation (LDKT) compared to deceased donor kidney transplantation (DDKT), has seen a surge over past few decades. Multiple factors of a living donation including the status of a health kidney compared to a DDKT and minimal ischemia time and surgical procedure improvements.

According to initial Renal Allograft function, Kidney Transplant patient could be divided into three groups; Immediate graft function (IGF), Slow graft function (SGF) and Delayed graft function (DGF).[2] DGF is a form of oliguric acute renal failure occurring in post-transplant period, and is often used synonymously with acute tubular necrosis.[3] DGF is defined as 'The Use of dialysis within 7 Days of renal transplant'. This definition offers a standard by which transplant centers can report outcomes.[4]

Slow graft function (SGF) defined as 'serum creatinine ≥3 mg/dL on 5th day post transplantation without requirement of hemodialysis'.

The incidence of DGF in LDKT has been reported to be 4-10%.[5] It is rare in LDKT and its incidence and leading factors have not been established.[6] Studies conducted in this regard have provided variable results. A study conducted in Turkey in 1998 showed incidence of DGF in LDKT 8.8%.[7] Another study from India showed that 7.1% of patients developed DGF.[5] A study from United States to determine the incidence and factors leading to SGF and DGF in LDKT showed incidence of 10.7% and 4.7% respectively and of IGF 84.6%.[8] Effects of delayed graft function are typically seen as graft rejection, patient and graft survival, including hospitalizations.[9-10] It is a major obstacle for allograft survival as it can be compounded by acute rejection and chronic allograft nephropathy. Patients developing SGF have a worse outcome than patients with IGF but similar or better than patients developing DGF in DDKT.

Even mild to moderate post renal transplant dysfunction can have a negative impact in graft function and survival.[1] A number of leading factors and their frequencies have been reported in various studies for SGF and DGF in LDKT, like female donor (IGF:44%, DGF:78%)[7], greater donor age (>50 years; IGF: 20%, SGF: 13%, DGF:32%) [8], Higher recipient/donor weight ratio (1.26) 7, recipient BMI (>30Kg/m2)[11], greater warm ischemia time (WIT) (>30 min; IGF:47%, SGF:65%, DGF: 55%)[8] and diabetic etiology of end stage renal disease (IGF: 16%, SGF:26%, DGF:45%).[8] Donor age >50 years emerged as an independent factor for rejection. One hypothesis is that kidneys from older donors may tolerate procurement and transplantation less well, sustaining greater injury thereby predisposing to DGF and rejection.[8]

The increased risk of DGF among female donors or donors with lower body weight may be related to smaller nephron mass.[7] Warm ischemia time is a potentially modifiable insult to transplanted kidney.[12] Few studies that evaluated the effect of longer WIT suggested an increased risk of DGF as well as poor long-term function.[13]

In our country LDKT is the only option as cadaveric (or deceased donor) program does not exist. There is no data in Pakistan about incidence of delayed graft function and its leading factors.
Identification of later will help in planning future preventive strategies before and during intraoperative period.

Subjects and Methods:

It was a Descriptive study, conducted at Department of Transplantation, Sindh Institute of Urology and Transplantation, from 22nd October 2019 to 23rd April 2020.

The total population size of kidney transplant in 6 months is approximately 240 patients. From previous reference study estimate of DGF is 4.7%8 with margin of error 3.3% and 95% confidence level, a total of 158 transplant patients were required for this study. Non-Probability consecutive sampling technique was applied for sample collection.

Inclusion Criteria

☐ Patients undergoing first Living Donor Renal Transplants of both genders
☐ Recipient age 18-50 years

☐ ESRD due to all causes

Exclusion Criteria

Following were excluded as available on medical record

☐ Acute graft rejection on Renal Biopsy
☐ Graft Arterial or Venous Thrombosis within 48 hours of transplantation.
☐ Second Renal Transplant
☐ Mechanical causes like Lymphocele
☐ Pyelonephritis
☐ CNI Toxicity

Data collection procedure

This study was conducted after approval from College of physicians and surgeons Pakistan. Consenting cases as defined in operational definition and all those meeting inclusion criteria were enrolled in the study from Department of Transplantation, SIUT. Informed consent was obtained from all patients for assigning them to sample and using their data in research.

All those patients who underwent Renal Transplantation from a living donor, from 18 to 50 years of age were recruited in the study. The data related to donor factors (Age, Gender, BMI), recipient factors (Age, Gender, BMI & cause of ESRD), and transplant factor (Warm ischemia time) were noted in pre-designed proforma. After transplantation serum creatinine was checked on day 01 of renal transplant and followed till day 10. Serum Creatinine was measured by Jaff Kinetic method. All the transplant patients were grouped on the basis on serum creatinine and need of dialysis within one week post transplantation, either IGF, SGF or DGF, after excluding the factors mentioned in the exclusion criteria. When serum creatinine will remain raised in early post-transplant period while monitoring daily serum creatinine levels, ultrasound and Doppler examination of graft was done. In the absence of technical or mechanical complication, graft biopsy was performed. Biopsy proven acute graft rejection were excluded from the study.

Similarly graft arterial and venous thrombosis diagnosed on Doppler ultrasound was also excluded.
The frequency of SGF & DGF was noted after early post-transplant period. The leading factors evaluated for the SGF & DGF were compared with IGF.

Data analysis procedure

All the data were entered and analyzed in SPSS.V.20. Descriptive statistics was computed for summarizing the continuous and categorical variables. Continuous variables like age, height, weight, BMI, WIT, and serum creatinine was presented as mean and standard deviation and their mean difference was determined among IGF, SGF and DGF using ANOVA /or Kruskal-Wallis test. While categorical variables such as gender, cause of ESRD, IGF, SGF, DGF, age (>50 years), BMI (>30Kg/m2) & WIT (>30minutes) was presented as percentages and frequencies.

Stratification was performed on IGF, SGF and DGF by age, gender, weight, BMI for donors and recipients separately. After stratification Chi-Square test was applied. P-value ≤ 0.05 considered as significant.

Results

The age height, weight and BMI of recipients and donors given in Table 1. BMI >30kg/m2 was found in only 2 (1.3%) recipients. Only 9 (5.7%) donors had >50 years age whereas female gender as donor was reported as 65 (41.1%).

The causes of ESRD showed that most of the patients had unknown cause 113 (71.5%) followed by infective/obstructive cause in 20 (12.7%), glomerular disease 17 (10.8%), cystic/congenital in 5 (3.2%), obstetric complication in 2 (1.3%) and HTN in 1 (0.6%) patient.

The serum creatinine level during first week are given in Table 2. The mean warm ischemia time (WIT) was 1.01 ±1.36. None of the patient had WIT of >30. Immediate graft function (IGF) was found in 154 (97.50%) patients, slow graft function (SGF) in 3 (1.9%) and delayed graft function (DGF) in 1 (0.6%) patient. A significant association of IGF was found with SGF (p-value <0.001) and DGF (p-value <0.001). (Table 3) Comparison was done to see the effect of IGF, SGF, and DGF with the general characteristics. Results shown in detailed in tables 4-6.

An insignificant mean difference of IGF, SGF, and DGF was observed with respect to baseline characteristics of donors and recipients (p value >0.05).
The combined findings of graft function (IGF, SGF, and DGF) also showed insignificant association with baseline characteristics of donors and recipients (p-value >0.05).
An insignificant association of IGF, SGF and DGF was found with causes of ESRD (p value 0.365).

Table 1: Age, height, Weight and Body Mass Index of Recipients and Donors (n=158)

Parameter (mean ±SD)	**Recipient** (Range ±SD)	**Donor**(Range ±SD)
Age in years	18-50 (30.08±7.37)	19-56 (32.15±8.68)
Height in Meter	1.39-1.85 (1.65±0.08)	1.37-1.90 (1.64±0.10)
Weight in Kg	30.9-85.3 (58.03±1.68)	38.9-101 (66.73±12.55)
BMI Kg/m^2	14.2-32.2 (21.21±3.69)	16.1-34.6 (24.88±4.03)

*BMI=Body mass Index

Table 2: Serum creatinine level with respect to days (n=158)

Serum Creatinine	**Mean ±SD**	**Minimum**	**Maximum**
Day 1	2.39 ±10.04	0.51	5.63
Day 2	1.42 ±0.73	0.42	4.70
Day 3	1.31 ±0.67	0.48	4.91
Day 4	1.25 ±0.69	0.41	5.58
Day 5	1.22 ±0.67	0.39	5.57
Day 6	1.21 ±0.69	0.35	5.63
Day 7	1.20 ±0.63	0.1	6.09

Table 3: Comparison of immediate graft function with respect to delayed and slow graft function (n=158)

SGF	IGF (no)	IGF (yes)	Total	p- value
No	1	154	155	<0.001
Yes	3	0	3	
Total	4	154	158	

*SGF= Slow Graft Function, DGF= Delayed Graft Function, IGF= Immediate Graft Function

Table 4: Comparison of slow graft function with respect to general characteristics (n=158)

	SGF	Yes n(%)	No n(%)	P value
Donor Age	**>50 years**	0	3(100)	0.667
	<50 years	9 (5.7)	148 (94.3)	
Donor Gender	**Female**	1 (33.3)	2 (66.7)	0.402
	Male	64 (41.3)	91 (58.7)	
Recipient age	**> 30 years**	2 (66.7)	1 (33.33)	0.391
	< 30 years	65(41.9)	90 (58.1)	
Recipient Gender	**Female**	0	3(100)	0.407
	Male	29 (18.7)	126 (81.3)	
Recipient BMI	**>30 kg/m2**	0	3(100)	0.843
	<30 kg/m2	2 (1.3)	153 (98.7)	
Donor BMI	**>30 kg/m2**	0	0	0.544
	<30 kg/m2	17 (11)	138 (89)	
WIT	**>30 sec**	0	1(100)	
	<30 sec	0	157 (100)	

*SGF= Slow Graft Function, BMI= Body Mass Index, WIT= Warm Ischemia Time

Table 5: Comparison of delayed graft function with respect to general characteristics (n=158)

	DGF	Yes n(%)	No n(%)	P value
Donor Age	**>50 years**	0	1(100)	0.805
	<50 years	9 (5.7)	148 (94.3)	
Donor Gender	**Female**	0	1(100)	0.781
	Male	65 (41.4)	92 (58.6)	
Recipient age	**> 30 years**	0	1(100)	0.389
	< 30 years	67 (100)	90 (98.9)	
Recipient Gender	**Female**	0	1(100)	0.634
	Male	29 (18.5)	128 (81.5)	
Recipient BMI	**>30 kg/m2**	0	1(100)	0.910
	<30 kg/m2	2 (1.3)	155 (98.7)	
Donor BMI	**>30 kg/m2**	0	0	0.728
	<30 kg/m2	17 (10.8)	140 (10.8)	
WIT	**>30 sec**	0	1(100)	
	<30 sec	0	157 (100)	

*DGF= Delayed Graft Function, BMI= Body Mass Index, WIT= Warm Ischemia Time

Table 6: Comparison of immediate graft function with general characteristics (n=158)

	IGF	Yes	No	P value
Donor Age	**>50 years**	9 (5.8)	0	0.805
	<50 years	145 (94.2)	4 (100)	
Donor Gender	**Female**	64 (41.6)	1 (25)	0.506
	Male	90 (58.4)	3 (75)	
Recipient age	**> 30 years**	65 (42.2)	2 (50)	0.756
	< 30 years	89 (57.8)	2 (50)	
Recipient Gender	**Female**	29 (18.8)	0	0.337
	Male	125 (81.2)	4 (100)	
Recipient BMI	**>30 kg/m2**	2 (1.3)		0.819
	<30 kg/m2	152 (98.7)	4 (100)	
Donor BMI	**>30 kg/m2**	17 (11)		0.482
	<30 kg/m2	137 (89)	4 (100)	
WIT	**>30 sec**	0	0	
	<30 sec	154 (100)	4 (100)	

*IGF= Immediate Graft Function, BMI= Body Mass Index, WIT= Warm Ischemia Time

Discussion

According to the current study findings, IGF was found in 154 (97.50%) patients, SGF in 3 (1.9%) and DGF in 1 (0.6%) patient. A number of leading factors and their frequencies have been reported in various studies for SGF and DGF in LDKT, like female donor (IGF:44%, DGF:78%)[7], greater donor age (>50 years; IGF: 20%, SGF: 13%, DGF:32%) [8], Higher recipient/donor weight ratio (1.26) 7, recipient BMI (>30Kg/m2)[11], greater warm ischemia time (WIT) (>30 min; IGF:47%, SGF:65%, DGF: 55%)8 and diabetic etiology of end stage renal disease (IGF: 16%, SGF:26%, DGF:45%).[8]

In our study, only 9 (5.7%) donors had >50 years age. It is reported that donor age >50 years emerged as an independent factor for rejection. One hypothesis is that kidneys from older donors may tolerate procurement and transplantation less well, sustaining greater injury thereby predisposing to DGF and rejection.[8]

The increased risk of DGF among female donors or donors with lower body weight may be related to smaller nephron mass.[7] In our study 65 (41.1%) donors were female. According to our study finding, the mean WIT was 1.01 ±1.36 whereas none of the patient had WIT of >30. Warm ischemia time is a potentially modifiable insult to transplanted kidney.[12] Few studies that evaluated the effect of longer WIT suggested an increased risk of DGF as well as poor long-term function.[13]

In a large, retrospective cohort study of kidney transplant recipients with a median follow-up seven years, SGF was associated with a higher risk of long-term graft failure similar to the DGF group, and all-cause mortality similar to IGF. SGF may be considered in between the IGF and DGF where current definitions of DGF cannot correctly identify it presence.[14]

Understanding of the concept of SGF into post-transplantation care and highlighting it as a distinct phenotype may help to improve graft survival by more closer look at the clinical status and therapeutic decisions.[15] Humar et al. proposed the concept of SGF with similar findings of similar survival as DGF

in a follow up study.[16-17] SGF may be associated with poor graft survival due to physical factors during organ procurement and its process causes oxidative stress and stimulation of renal limited inflammatory responses.[18]

Our study had several important limitations. First, our study was cross-sectional in nature, and so, as with all observational studies, causality cannot be inferred. Second, our study did not include all potential covariates which might influence graft, such as, recipient socioeconomic status.

Conclusion

The frequency of DGF was found to be 0.6% and SGF 1.6% among living donor kidney transplants. The leading factors to slow graft function and delayed graft function studied in previous studies were not found significant in our study probably because of small sample size of our study.

Conflict of Interests: None Declared

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