Original Research Article

Pre Renal Assessment For A Successful Kidney Transplant

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Abstract

Introduction: Living donor kidney transplantation is the treatment of choice for patients with end stage kidney disease, which prevents chronic dialysis and its long term side effects. In addition to the detailed clinical history and thorough laboratory testing, anatomical assessment of kidneys, pre donation kidney volume and its function before transplantation are important factors to assess post transplant outcome. **Materials and methods:** Patients undergoing first renal transplant and those between age group of 18 to 60 years were included in the study. Donor kidney volume was measured ultrasonographically, from which donated kidney volume was calculated to evaluate GFR of the donated kidney from the total GFR of the donor. Estimation of recipient graft function was done using four variable abbreviated MDRD equation at 3, 6, 9 and 12 months post transplant. **Results :**Correlation of the donor age and donor kidney volume with recipients eGFR was done and the results were tabulated. Statistical analysis was done and correlations were seen with Pearson's correlation coefficient. Statistical significance was defined as p value 0.05. **Conclusion:** Living donor kidney transplantation remains one of the vitally important treatment option for the end stage renal disease patients. Estimation of donor kidney volume, eGFR and donor age all together play an important role in post transplant graft survival and also better renal outcomes and functioning.

Keywords : Donor, Glomerular Filtration Rate, Recipients.

Introduction

Increasing incidence of End Stage Renal Disease worldwide is a matter of concern. Treatment option for these patients are haemodialysis and renal transplantation. Successful renal transplantation means both short and long term normal or near normal renal allograft function. Potent immunosuppressive regimens are now available to improve the short term renal allograft outcome [1]. But the long term graft survival remains suboptimal.

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The quality of the donated organ kidney, its function before transplantation and the age of the donor have significant impact on the functioning of the grafted kidney. It has been hypothesised that the size and pre-transplant glomerular filtration rate (GFR) of a donated kidney influence post- transplant outcomes[2]. It has been seen that, renal grafts donated from male to female are far better than grafts from female to male. This has been attributed to differences in size, but without careful study of the direct size measurements[3]. Also some evidences suggest that higher pre-donation GFR correlates positively with post-transplant outcomes.

This study is aimed at, to examine the association between donor kidney volume, donated kidney GFR and age of the donor with recipient's eGFR at various months after live related renal transplantation. This will

help to judge the effectiveness of transplantation in both short and long term basis.

Materials and Methods

This is a prospective study, conducted between October 2019 to March 2020, for a period of one and half year. 53 live kidney donors and their recipients were studied . Cases included in this study were first renal transplant, recipients within the age group of 18 to 60 years, willingness to participate as indicated by a signed written consent. Cases excluded were cadaveric transplant, unrelated donor and those not agreeing for transplantation. Detailed clinical history was taken and a thorough medical checkup was undertaken in each and every case.

Measurement of donor kidney volume

Donor kidney volume was measured by the Siemens P4 Ultrasound machine. This was conducted by experienced Radiologist.
Length (L) was defined as maximum craniocaudal distance, Width (W1 x W2) were defined as the maximum distance in between the two transverse dimensions.
These parameters were measured 15 days before the due transplant date and the kidney volume was calculated as per the formula given below.

$$V = 0.49 * L * W1 * W2$$

Total kidney volume for each donor was taken as left kidney volume + right kidney volume

$$\text{Percentage of donated kidney volume} = \frac{Transplantedkidneyvolume * 100}{Totalkidneyvolume}$$

Percentage of the donated kidney volume (% DKV) was taken in order to calculate the GFR of the donated kidney from the total GFR of the donor.
The volume of the single transplanted kidney was then corrected for recipient body surface area (BSA) to calculate the corrected donated kidney volume.

$$\text{Corrected donated kidney volume} = \frac{donatedkidneyvolume * 1.732}{RecipientBSA}$$

This adjustment is needed in order to assess the effects of the transplanted graft volume in a particular recipient.

Measurement of donor GFR

Donor total GFR was measured by the 99m Tc- DTPA (diethylenetriamine pentaacetic acid) two plasma sample method. DTPA GFR was then corrected for the donor body surface area and expressed as ml/ min/ 1.73 m^2. Donor GFR was also measured by the four variable Abbreviated MDRD Equation 15 days prior to the due transplant date.

Estimation of recipient graft function

Graft kidney function was measured by the four-variable Abbreviated MDRD Equation at 3 months, 6 months, 9 months and 12 months post transplant.

$$eGFR = 186 * (SCr)^{-1.154} * (age)^{-0.203} * 0.742(if female) * 1.212(if African - American)$$

Donor age, donated kidney GFR and corrected donated kidney volume were then correlated with the recipient estimated GFR at 3 months, 6 months, 9 months and 12 months after the renal transplantation.

Statistical analysis

The recipient data was stratified as per the following parameters:

1. Corrected donated kidney volume: < 90 mm^3/ 1.73 m^2 vs≥ 90mm^3/1.73 m^2.
2. Donated kidney GFR: < 40 ml / min / 1.73 m^2 vs ≥ 40 ml / min/ 1.73 m^2
3. Donor age: < 45 years. vs ≥ 45 years

Statistical analysis was performed by using software version 15. 0 (Chicago,IL). Data were expressed as mean ± SD (minimum-maximum) or as n (%) when appropriate. Student t-test and / or ANOVA test to compare means for parametric data. Correlations were seen with Pearson's correlation coefficient. To further characterise the effects of different donor variables and recipient factors on graft function at 3 months, 6 months, 9 months and 12 months post transplantation we performed uni-variable and multi variable linear regression analysis. Statistical significance was defined as p- values < 0.05.
This clinical study was approved by the Ethics Committee.

Results

A total number of 76 patients had undergone allogenic renal transplantation from October 2019 to March 2020 in our institute. Out of these, 23 were excluded due to various reasons as per the exclusion criteria. Finally 53

patients of ESRD who underwent renal transplantation within the above mentioned period were included in the study.

Basic diseases of the recipients included, presumed Chronic glomerulonephritis 34(0.64%), presumed Chronic interstitial nephritis13 (0.24%), diabetic nephropathy 04 (0.07%), lupus nephritis 01 (0.01%), Adult polycystic Kidney disease01 (0.01%). HLA study of both the donor and recipients was done. HLA mismatch was calculated from four alleles of the HLA-A, HLA-B locus.(Figure-1). All these patients were on triple drug immunosuppressants. 45 (84.9%) were on Tacrolimus and 08 (15.1%) were on cyclosporine; 46 (86.8%) patients were on MMF and 07 (13.2 %) patients were on Azathioprene. The dosage varied according to specific requirements. All patients had received steroids. 11 (20.8 %) patients received induction therapy with IL-2R receptor blockers (One case received Basiliximab and 10 received Daclizumab).

The baseline recipient characteristics were noted down. Amongst the 53 cases studied, the overall age of the patients was 34 ± 10.6 years. There were 48 males with a mean age of 34.3 ± years and 05 females with a mean age of 31± 10. 2 years. The mean BSA of the recipients was 1.57± 0.13 kg / m^2.

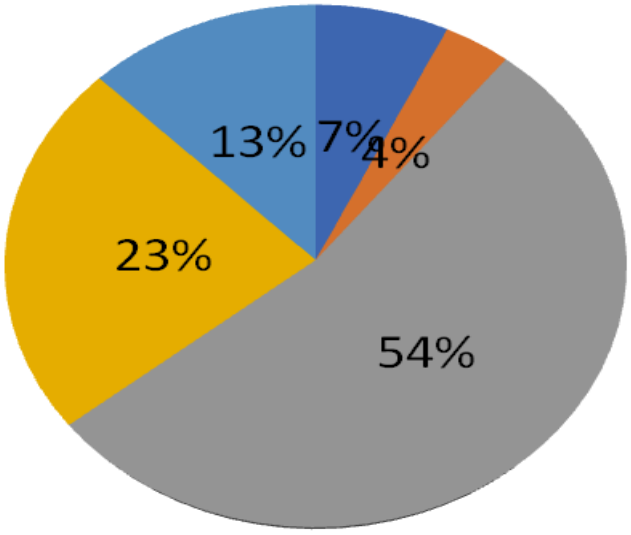

Figure-1: Number of HLA Mismatches (%)

The baseline donor characteristics were listed. There were 15 male and 38 female donors. The overall mean age of the donors was 41.4 ± 11.9 years. The mean total GFR of the donors as calculated by the 99m Tc – DTPA (diethylene triamine pentaacetic acid) two plasma sample method was 94 ±14.6 ml/ min / 1.73 m^2. The mean donated kidney volume was 83.5 ± 14.8 mm^3. The mean of the percentage of the donated kidney volume was 50.2 ± 3.9%. The donor kidney volume corrected for recipient body surface area was 93 ± 22.7 mm^3. The donated kidney GFR was 47.3 ± 8.6 ml/ min / 1.73 m^2. Estimated GFR (eGFR) of the recipient after transplantation was calculated by the Abbreviated MDRD 4 variable equation at 3, 6, 9 and 12 months respectively after the renal transplantation. The mean eGFR at the end of 3 months was 84.6 ± 23.4 ml/ min / 1.73 m^2. It was 80.2 ± 20.5 ml/ min / 1.73 m^2 at the end of 6 months, 78.8 ± 21.3 ml/ min/ 1.73 m^2 at the end of 9 months and 77.8 ± 17. 6 ml / min / 1.73 m^2 at the end of 12 months. (Table-1).

Correlation of the Corrected Donor Kidney Volume with the eGFR of the recipient was done, for which the

recipients were divided into two groups (Figure-2). In group 1, there were 24 recipients having corrected kidney volume < 90 mm^3 and in the group 2, there were 29 recipients, having corrected kidney volume ≥ 90 mm^3. It was seen that the recipients in group 2 had better eGFR at 3 and 6 months, although the difference was not seen at 9 and 12 months. Correlation of the donated kidney GFR with eGFR of the recipients was noted down (Figure-3). The mean donated kidney GFR was 47 ± 8.6 ml/ min/ 1.73 $m^{2.}$ In group 1, there were 17 recipients, who received donated kidney GFR of < 40 ml/ min/ 1.73 m^2 and in group 2, there were 36 recipients, who received donated kidney GFR ≥ 40 ml/ min / 1.73 m^2. It was seen that the recipients in group 2, had a significantly higher GFR at 6 months, but not thereafter. Correlation of the donor age with eGFR of the recipients showed (where 33 recipients were having donor age under 45 and 20 recipients with donor age ≥ 45 years), no difference in the recipients eGFR at 6 and 9 months respectively, but there was a significant difference in the mean eGFR between the two age groups at 3 months and at the end of 12 months (87.8 ± 20.4 vs 79.6 ± 27.4 ml/ min and 82.7 ± 16.8 ml/ min vs 71 ± 15.8 ml/ min) respectively. (Figure-4) (p = 0.049 and p= 0.04).

Univariate analysis of factors associated with eGFR of the recipients at various months post transplant were tabulated. We found that recipient's eGFR at 3 months was associated with the age of the donor and the corrected donor kidney volume. At 6 months, the recipient's eGFR was associated with corrected donor kidney volume and donated kidney GFR. At 9 months, we could not find any association of the recipient GFR with the various donor factors. However, there was a negative association between the recipient eGFR at 12 months with the age of the donor and a positive correlation with the percentage of the donated kidney volume. In multivariate analysis, donor factors analysed were similar as that of univariate analysis. (Table - 2)

Correlation of the recipient's eGFR at various post transplant months with different parameters showed a negative correlation between the donor age and GFR of the recipient .
At 3 and 12 months (p= 0.02, 0.04) respectively, but failed to statistically correlate during 6 and 9 months post transplant. Corrected donor kidney volume was found to have a positive correlation with the recipients GFR at 3 months and 6 months, but not at 9 and 12 months. Similarly the donor GFR correlated with the recipient GFR at 6 months, but not during the subsequent follow up. We also estimated the GFR of the donor by the four variable abbreviated Modification of Diet in Renal Disease (MDRD) equation. The results of both the mean estimated GFR and GFR done by DTPA methods were almost similar (99.5 ± 26.7 vs 94 ± 14 ml / min / 1.73 m^2). Similarly mean donated kidney GFR by MDRD equation and DTPA method were 49.7 ± 12 vs 47.3 ± 8.6 ml/ min/ 1.73 m^2.

Table - 1 : Serial eGFR of the recipients during follow up

Time period post transplant	eGFR (ml/min/1.73 m^2)
At 3 months (n = 53)	84.63 ± 23.4
At 6 months (n = 53)	80.2 ± 20.45
At 9 months (n= 53)	78.82 ± 21.33
At 12 months (n = 36)	77.80 ± 17.6

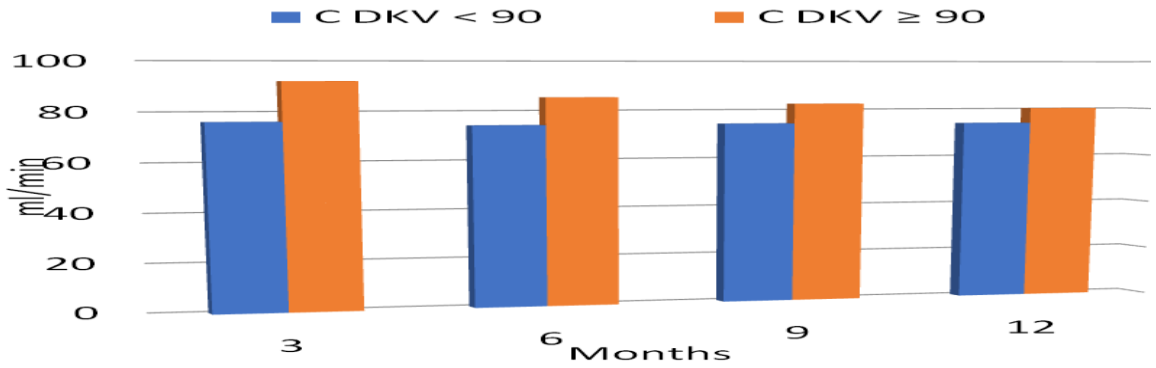

Figure-2: Corrected DVR and e GFR

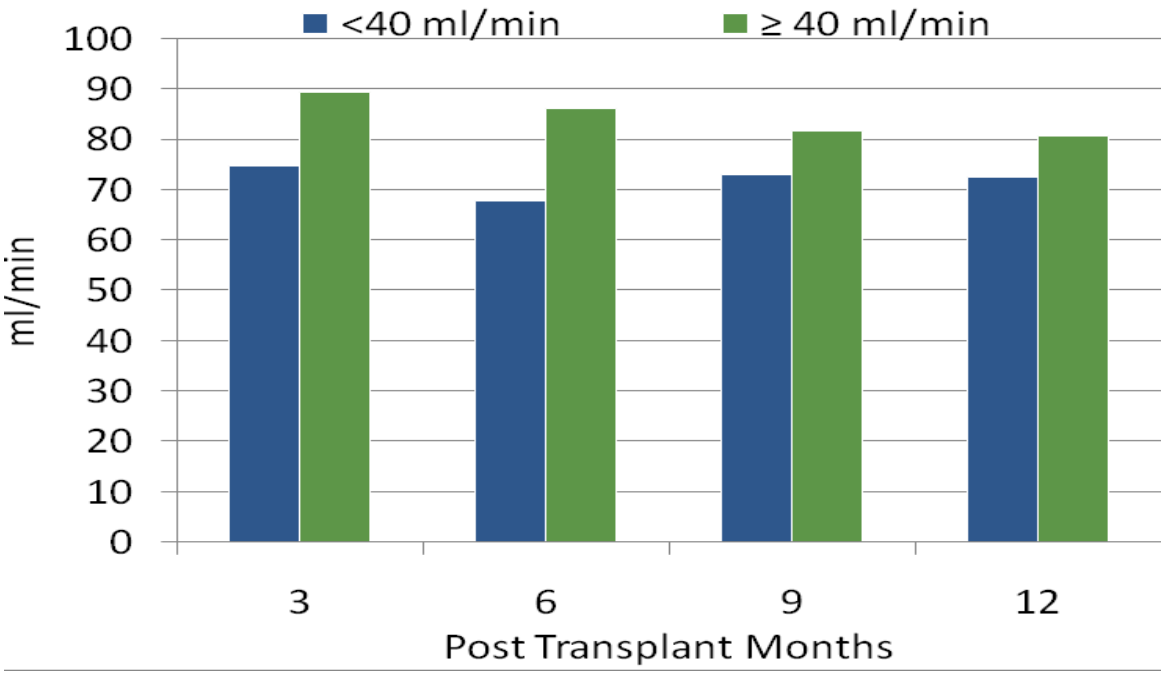

Figure-3: Donated Kidney GFR and eGFR at various post transplant Months

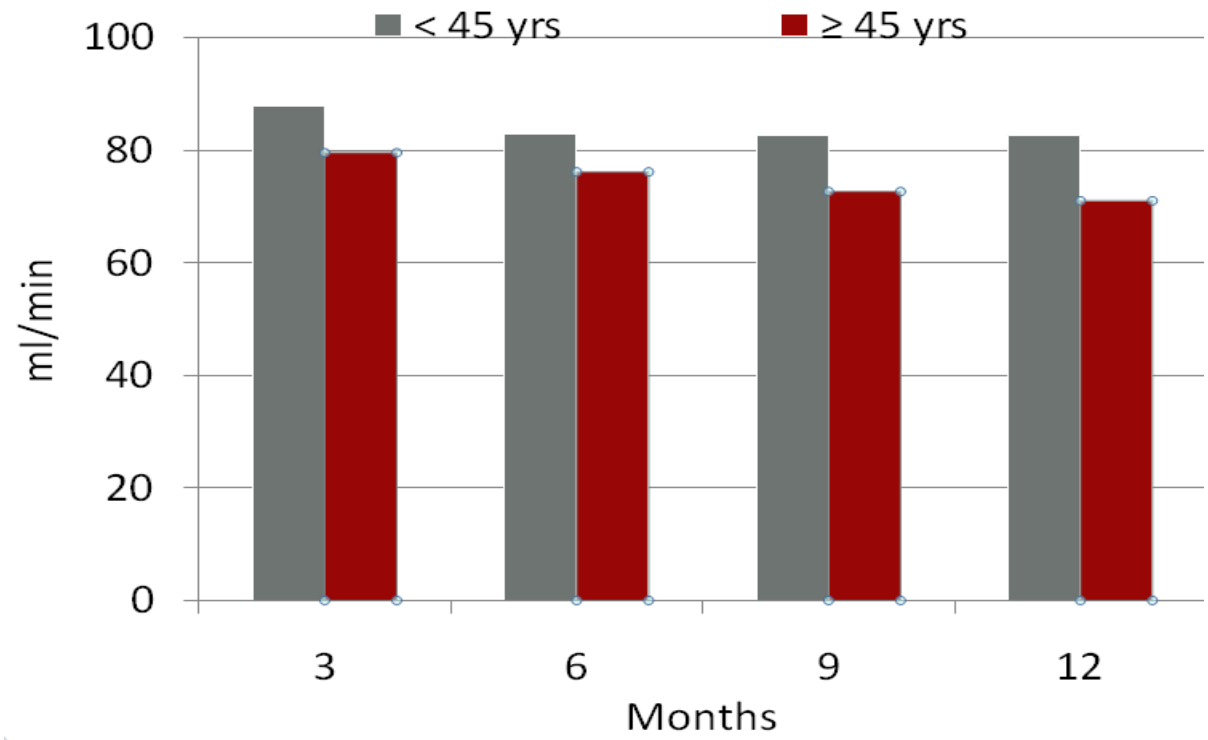

Figure-4: Donar age and e GFR

Table - 2 : Univariate and Multivariate analysis of factors associated with eGFR of the recipient at various post transplant months

3month	Univariate ( )	P value	Mult. Var. ( )
D. age	-0.543	0.049	0.024
Sex	3.117	0.675	0.170
%DKV	1.115	0.182	0.269
Corr.DKV	0.303	0.033	0.016
DKGFR	0.709	0.063	0.128
6 month	Uni.var ( )	P value	Mult.var.(p)
D.age	-.309	0.196	0.695
Sex	0.395	0.950	0.893
%DKV	0.320	0.093	0.20
Corrr.DKV	0.310	0.012	0.034
DKGFR	1.003	0.002	0.004
9 month	Uni.var ( )	P value	Multi.var.(p)
D.age	-0.342	0.170	
Sex	6.9710.290		
%DKV	1.221	0.108	
Corr.DKV	0.127	0.336	
DKGFR	0.425	0.227	
12 month			
D.age	-.538	0.027	0.056
Sex	1.708	0.783	0.523
%DKV	2.266	0.013	0.02
Corr.DKV	-3.00	0.840	0.129
DKGFR	0.419	0.224	0.970

Discussion

Outcomes of renal transplantation depends on both immunological and non immunological factors. Among the non immunological factors, primary kidney disease and post transplant infections are extensively studied. Donor age plays an important role with recipient's

eGFR. Kidney function declines progressively with age, leaving a tendency for other age related donor factors to exist with low GFR [4].The mean age of donors in the present study was 42.4 ± 11.9 years. We found a strong negative association between the donor age and the recipient GFR at 3 and 12 months.Our results are consistent with those of Poggio et al, who found that younger age of the donor was associated with higher GFR. The mean age of donors in their study was similar to that in our study 43 ±9 years. Further they found that recipients with donors aged less than 45 years had significantly better GFR at 6 months, one to two years post transplant [5].When we divided our recipients on the basis of the donor age into those < 45 years (group 1) and > 45 years (group 2) we found that at the end of the study period at 12 months, the mean eGFR of recipients in group 1 was significantly better with a value of 82.7 ± 16.8 ml/ min/ 1.73m^2vs 71± 15 ml/ min/ 1.73 m^2). In the Norwegian experience graft survival was about 65% after 4 years with older living donors versus 85% with younger donors[6]. The effect of donor age on patient survival persisted even when censoring recipients in whom grafts failed before death suggesting that both longevity and quality of graft function are important in patient survival[7]. The French cohort study also noted that baseline eGFR was associated with age, leading the authors to conclude that baseline values < 90 mL / min/1.73m^2 are reasonable for older donors[8].

Recipients receiving larger corrected donated kidney volume have definitely better outcome. Those who received corrected kidney volume ≥ 90 mm3 had significantly higher GFR at 3 months (92 vs 76 ml/ min/ 1.73m^2) and at 6 months (85 ml vs 74 ml/ min / 1.73 $m^{2)}$ respectively. Our results are consistent with those of Poggio et al, 2006 who also found a correlation between the measured kidney volume and GFR. However, they had taken a cut off of measured kidney volume as 120 mm^3, which may be valid for western population where the body surface area is much larger in comparison to that of Indian population. With a smaller body surface area of our donors, a cut off of 90 mm^3 should be valid. The mean body surface area of the donors in the study by Poggio et al was 1.86 ± 0.22 m^2, in contrast to 1.55 ± 0.1m^2 of our patients. Also majority of our donors were females (71%) who had lower body surface area of 1.5 ± 0.18 m^2 as compared to that of the recipients , majority of whom were males. So our donors had a smaller body surface area compared to our recipients. In a study of 54 live related renal transplantation, Saxsena et al also found a correlation of recipient GFR with donor kidney volume/ weight ratio at 6 and 12 months post transplant[3]. Douverny JV found that the kidney weight had a correlation with the donor's BMI (r= 0.43, p < 0.001) and with the Creatinine clearance at 12 months (r= 0.31, p= 0.001). They concluded that kidney weight significantly influences the Creatinine clearance at 12 months after transplantation[9]. Narasimhamurthy et al studied 85 donors and found those with larger combined volumes were more likely and quickly to achieve eGFR values of 60 mL/min/ 1.73 m2or more[10]. Results of the current study also showed that, recipients receiving larger corrected donated kidney volume ≥ 90 mm^3 had better eGFR at 3 and 6 months, though the difference was not seen at 9 and 12 months post transplant . The most recent international guideline on living kidney donor and care recommends using serum creatinine - based equations and then to confirm GFR via different techniques.[11]

Over the past decades, the selection criteria for living kidney donors has become more restrictive with the minimum baseline level of kidney function in living donors[12]. In this study, donated kidney GFR and eGFR of the recipients were analysed. To study the correlation, the patients were divided into group 1 (n =17) having GFR < 40ml/ min / 1.73 m^2 , group 2 (n = 36) having donated kidney GFR ≥ 40 ml / min / 1.73 m^2. Recipients in group 2 had significantly higher GFR at 3 months (89 vs 75 ml/ min / 1.73 m^2) and at 6 months (86 vs 67 ml/ min / 1.73 m^2). Lezaic et al studied 180 live kidney recipients with a functioning graft > 1 year with an aim to estimate the relationship between the single kidney GFR of the transplanted kidney with subsequent graft function. They assigned patients in group 1 to those, who received single kidney GFR < 50ml (32 patients) and group 2, to those who received single kidney GFR > 50 ml (38 patients). They found no correlation of single kidney GFR on the graft outcomes[13]. Our results though not entirely agree with Lezaic et al, still reflects the same findings that the donated kidney GFR though has impact at 3 months and 6 months GFR of the recipient, but still fades at 9 and 12 months post transplant. In a study of 344 live related renal transplantation by Norden et al, it was seen that graft survival was significantly decreased in recipients of graft from donor having low GFR[14]. In 2011, Brar et al showed that majority, that is 66% of centres used a cut-off value of GFR of > = 80 mL/ min for exclusion of living kidney donors[15]. Young et al compared the recipients of living donor kidneys with eGFR < 80ml/ min/ 1.73m^2 to those ≥ 110 ml/ min / 1.73m^2 , followed them up to 6 years and found the hazard ratio for the outcome of graft loss to be 1.23(

95% Cl0.84-1.92, p= 0.26)[16]. Some centres used creatinine clearance as a measure of eGFR followed by isotopic clearance assay[17].In our study, we found that the donor mean eGFR (MDRD) and GFR done by 99m Tc-DTPA (diethylenetriamine pentaacetic acid) were almost similar. Also mean eGFR and DTPA GFR of the donated kidney were similar. However, we didn't find any statistically significant correlation between eGFR of the recipient and donor GFR as estimated by MDRD equation. This may be due to smaller study population in our study group.

Conclusion

The present study includes 53 donor- recipient pairs with mean age of the recipient being 34± 10.6 years, who underwent live kidney transplantation at our institution. The characteristics of the donated kidney was corrected donated kidney volume: 93 ± 22.7mm3, donated kidney GFR (by DTPA) : of 47.86ml/ min and donated kidney eGFR (by MDRD Equation): 49.27± 12ml/min. Accordingly we concluded that recipients who received corrected kidney volume ≥ 90 mm^3 had better renal function at 3 and 6 months post transplant. Similarly when the GFR of the donated kidney was ≥40ml/ min, renal function at 3 and 6 months post transplant was significantly better. Donor age < 45 years resulted in significantly better graft function at 12 months post transplantation. So donor kidney size, donor GFR and age of the donor should be considered as predictive factors for graft outcome in living kidney transplantation.

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