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ORIGINAL ARTICLE

Age Combination of Living Donor and Recipient of Kidney Transplantation and Its Impact on Transplant Outcome; a retrospective study

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ABSTRACT

Background: Age has been found to be one of the most important factors affecting kidney transplant outcome. In our study, we evaluated the impact of combined age of living donor and recipient on kidney transplant outcome.
Methods: Retrospective cohort study conducted on 3068 kidney transplant recipients who underwent kidney transplantation at Mansoura Urology and Nephrology Centre between March 1976 and December 2019, divided into four groups according to recipient and donor age, group I: Kidney transplant recipients < 40 years from donors < 40 years (1665 kidney transplant recipients), group II: Kidney transplant recipients < 40 years from donors ≥ 40 years (932 kidney transplant recipients), group III: Kidney transplant recipients ≥ 40 years from donors < 40 years (320 kidney transplant recipients) and group IV: Kidney transplant recipients ≥40 years from donors ≥ 40 years (151 kidney transplant recipients). Results: Incidence of acute rejection and chronic rejection was higher in group I and of lower incidence in group VI. Incidence of post-transplant hypertension, diabetes, hepatic impairment and malignancy was higher in group III and lower in group II with statistical significant difference (p value <0.05). Overall, 5,10,15-year graft survival was better in group IV and worse in group II with statistical significant difference (p value <0.05). 5,10,15-year patient survival was better in group II and worse in group III with statistical significant difference (p value <0.05).
Conclusion: Young donor to young recipient transplantation was associated with higher incidence of rejection. Old donor to young recipient transplantation was associated with the best patient survival, lower incidence of post-transplant medical complications but the worst graft survival. Young donor to old recipient transplantation was associated with higher incidence of post-transplant medical complications and malignancy and worst patient survival. Old donor to old recipient transplantation was associated with the lowest incidence of rejection and the best graft survival.
Keywords: kidney transplantation, age, graft survival.

INTRODUCTION

Renal transplantation is the gold standard therapy for patients affected by end-stage renal disease (ESRD) followed by significant improvement of patients' quality of life (1). Renal transplantation is generally better than dialysis as it provides significant improvements in quality of life-related to health (2).
With increasing number of end-stage renal disease (ESRD) patients waiting for transplantation, the gap between the supply of available kidneys and the demand for them has been progressively increasing (3). So, donor selection criteria have been expanded to include non-heart beating donors and donors of advanced age (4). Older donors are more likely to be excluded from donation than younger donors on the basis of problems discovered during the medical evaluation. Donor age and its effects on short- and long-term outcomes of living donor kidney

transplant (KT) have been evaluated in many studies and demonstrated the negative impact of advanced donor age on graft function and survival (5).

Graft survival of the kidneys from younger donors has been found to be significantly better than that of kidneys from older donors (6). However, each case should be considered on individual merit and if the older donor is judged fit after rigorous medical evaluation, and if the renal function of the donor is normal after correction for age and gender, there is no compelling evidence for excluding donation on the basis of chronological age alone (7).

In light of the known decrease in glomerular filtration rate with advancing age, several studies have sought to establish the relation between donor age and allograft failure and function following live donor kidney transplant (LDKT) (8). Matas et al. (9), reported the outcome of 2,540 living donor kidney transplants in their center and documented worse outcome when the donor was >55 years of age (9). More recently, it has been shown that the benefit of older kidney transplants is linked to recipient criteria such as waiting time, cause of kidney failure, and age (10). Recipient age at time of transplantation has a clear correlation with long-term outcome as reported in both Europe and the United States of America (11).

With the increasing number of potential candidates for kidney transplantation, and the rising age of both recipients and the general population, older patients with end-stage renal disease (ESRD) who have no medical or surgical contraindications should be considered for kidney transplantation. There is no doubt that transplantation offers a survival advantage for the majority of older patients over remaining on dialysis (12). Kidney transplantation in old recipients has been considered as a big challenge requiring targeted evaluation with close monitoring and management (13). Old recipient age has been found to significantly decrease graft survival and increase incidence of death with a functioning graft compared to younger kidney transplant (KT) (14).

Recipient age has been considered by some investigators as an important modifier of the relationship between donor age and graft survival (5). The negative impact of donor age on incidence of acute rejection and graft survival has been found to be decreased by older recipient age and so, the impact of combined age of donor and recipient may be beneficial in predicting renal transplant outcomes (15) & (16).

Living donor transplantation has been shown to have better short- and long-term graft outcomes than those of deceased donor transplantation. However, factors impacting graft function from deceased donor (DD) have been studied thoroughly, while factors impacting graft function from living donor (LD) still remain unclear (17).

Unfortunately, most of the studies analysed the influence of either donor age or recipient age separately on renal allograft survival and few studies analysed the combined influence of donor age and recipient age on renal allograft survival are only for older donors and older recipients and most of the studies included data from deceased donors (18) & (19). In this work, we seek to evaluate the impact of combined age of living donor and recipient of kidney transplantation on patient and graft outcome. To the best of our knowledge, this is the first study that evaluates the impact of combined age of living donor and recipient of kidney transplantation on patient and graft survival using this large population and over this long period of time.

Aim of the Work: Our study aims to evaluate the impact of combined age of living donor and recipient of kidney transplantation on patient and graft outcome at Mansoura Urology and Nephrology Center.

PATIENTS AND METHODS

A retrospective cohort study held in Urology and Nephrology Center, Mansoura University, Egypt.

Ethical consideration: Our study is a retrospective study. Written informed consent was obtained from all participants. The study was approved by the research ethics committee of the Faculty of Medicine, Mansoura University. According to The Code of Ethics of the World Medical Association (Declaration of Helsinki), the study was done for studies involving humans. The data was retrieved from our patient information system at Urology and Nephrology Center after an agreement from the head of the center's department and director. We confirm that we do not use patients' names, initials, or hospital numbers. The medical research and ethics committee of Zagazig University approved the study. The work was carried out following The Code of Ethics of the World Medical Association.

Subjects: The study included all kidney transplant recipients (KTRs) received allo-renal transplantation (3068 KTRs) in the Urology & Nephrology Center, Mansoura University, Egypt, during the period between March 1976 and December 2019, the data were retrospectively analyzed. The patients were divided into 4 main groups according to recipient and donor age: Group I: Kidney transplant recipients < 40 years from donors < 40 years (1665 KTRs), Group II: Kidney transplant recipients < 40 years from donors ≥ 40 years (932 KTRs), Group III: Kidney transplant recipients ≥ 40 years from donors < 40 years (320 KTRs) and Group IV: Kidney transplant recipients ≥40 years from donors ≥ 40 years (151 KTRs).

The transplant registry at Mansoura Urology and Nephrology Center was reviewed for each group to assess the transplant outcome using univariate and multivariate analysis. Records of all kidney recipients were reviewed for peri-operative details including demographic data as (recipient age and sex, donor age and sex, and consanguinity), causes of end stage renal disease, dialysis duration, pre-transplant medical disorders (hypertension, diabetes mellitus, chronic liver disease) and immunologic data as regard HLA and DR mismatching, operative details including ischemia time and time to diuresis and post-operative details including (induction immunosuppressive drugs, maintenance immunosuppressive protocols, frequency of acute and chronic rejection episodes, acute tubular necrosis, post-transplantation medical disorders (hypertension, diabetes mellitus, liver impairment, viral infections, bacterial infections, malignancy), post-transplantation surgical complications (wound dehiscence, wound infection, hematoma, lymphocele), mean serum creatinine over 5 years post-transplant and condition of the patient at last follow up.

Immunosuppression Protocols: Patients received one of different regimens of induction therapy such as anti-thymocyte globulin (ATG) (1.5 mg/kg/day administered by IV infusion for 7 to 14 days), basiliximab (Simulect) (20 mg infused over 20-30 minutes by central or peripheral intravenous administration. The first 20 mg dose should be given within 2 hours prior to transplantation surgery. The recommended second 20 mg dose should be given 4 days after transplantation) and alemtuzumab (Campath 1-H) (60 mg by slow IV infusion on day zero). Then the recipients maintained on one of the following regimens of maintenance immunosuppression (Steroid-free protocol, Cyclosporine-based protocol, Campath protocol, Sirolimus-based protocol, Tacrolimus-based protocol).

Follow-up Data: During post-operative hospitalization, renal functions were monitored daily by serum creatinine, creatinine clearance, urine analysis and graft grey-scale ultrasonography and graft Doppler to evaluate graft perfusion and resistive index. After discharge, the recipients were regularly followed up in the outpatient clinic (twice weekly in the first month, once weekly in the second month, every other week until the end of the sixth month and monthly thereafter).

Statistical Analysis: The findings were recorded, tabulated and analyzed using SPSS for windows (SPSS Inc. Chicago). T test was used to compare the continuous data between the two groups. Categorical data were compared using Chi-Square test. The graft and patient survival were computed using the Kaplan-Meier technique. P-value < 0.05 was considered statistically significant and non-significant if >0.05.

RESULTS

There was a statistically significant difference among the 4 groups regarding demographic data. The rule in our center is living-related donors. Transplantation from unrelated donors occurred more frequent in group III (p-value <0.05) (table 1). Incidence of pre-transplant hypertension was higher among old recipients groups (group III, IV), with a statistically significant difference (p-value <0.05). The majority of patients underwent hemodialysis for variable duration, with no statistical significance among the studied groups (table 1). Most of patients were mismatched in 2 alleles of HLA class I, with higher prevalence among group I and II and the difference showed a statistically significant difference (p-value <0.05). The majority of patients were mismatched in 1 allele of HLA class II, with higher prevalence among group II and III (p-value <0.05) (table 1).

Most of patients received induction immunosuppressive therapy (Basiliximab was the commonly used type), with higher prevalence among recipients from old donors (group II, IV), with a statistically significant difference (p-value <0.05) (table 2). The majority of patients were maintained on triple immunosuppressive therapy, with higher

prevalence among old recipients (group III, IV), with a statistically significant difference (p-value <0.05). Steroid-based regimen was used in the majority of the recipients, with higher prevalence among recipients from young donors (group I, III), with a statistically significant difference (p-value <0.05). As regards Calcineurin inhibitors (CNI), most of the recipients in group III (old recipients from young donors) were maintained on cyclosporine-based therapy, with a statistically significant difference (p-value <0.05), while most of the recipients from old donors (groups II, IV) were maintained on tacrolimus-based therapy, with a statistically significant difference (p-value <0.05). Most of the recipients from old donors (groups II, IV) were maintained on Mycophenolate-based therapy, with a statistically significant difference (p-value <0.05) (table 2).

Incidence of acute rejection was less among group IV (old recipients from old donors) and more among group I (young recipients from young donors), with a statistically significant difference (p-value <0.05). The incidence of acute tubular necrosis was higher among group II, with no statistical significant among the studied groups. The incidence of chronic rejection was higher in group I and lowest in group IV, with a statistically significant difference (p-value <0.05) (table 3).

Most of the patients in group III developed post-transplant hypertension and group II had the least incidence, with a statistically significant difference (p-value <0.05). The incidence of post-transplant diabetes was higher among old recipients (group III, IV), with a statistically significant difference (p-value <0.05). The incidence of post-transplant malignancy was higher among group III, with a statistically significant difference (p-value <0.05). The incidence of post-transplant hepatic impairment also was higher among old recipients (group III, IV), with a statistically significant difference (p-value <0.05). Incidence of post-transplant bacterial and viral infections was higher among old recipients groups (group III, IV), with a statistically significant difference (p-value <0.05) (table 3).

The incidence of wound dehiscence was higher among old recipient groups (group III, IV), with a statistically significant difference (p-value <0.05). Post-transplantation lymphocele had higher prevalence among group III, with a statistically significant difference (p-value <0.05).The incidence of wound infection was higher among group III and group I, with a statistically significant difference (p-value <0.05) (table 4).

There was a statistically significant difference among the 4 groups regarding serum creatinine at the end of each year over 5 years post-transplant (table 5).

Overall, 5, 10 and 15 years graft survival was better in group IV and worse in group II, with a statistically significant difference (p-value <0.05) (figure 1).

Overall, 5, 10 and 15 years patient survival was higher in group II and lower in group III, with a statistically significant difference (p-value <0.05) (figure 2).

Table 1: Demographic data, baseline medical conditions, and immunologic workup:

	Group I 1665 KTRs No. (%)	Group II 932 KTRs No. (%)	Group III 320 KTRs No. (%)	Group IV 151 KTRs No. (%)	P-value
Recipient age mean±SD	25.97±8.28	23.27±7.19	45.88±4.87	47.58±4.87	***<0.05***
Recipient Sex: Male	1214(72.9%)	627(67.3%)	275(85.9%)	136(90.1%)	***<0.05***
Donor age mean±SD	30.16±5.26	48.06±5.78	31.02±5.14	46.09±5.60	***<0.05***
Donor Sex: Male	853(51.3%)	291(31.2%)	184(57.5%)	52(34.4%)	***<0.05***
Consanguinity: Related Unrelated	1392(83.6%) 273(16.4%)	877(94.1%) 55(5.9%)	203(63.4%) 117(36.6%)	138(91.4%) 13(8.6%)	***<0.05***
Hypertension	880(52.9%)	464(49.8%)	204(63.8%)	90(59.6%)	***<0.05***
Hepatitis C	300(18%)	158(17%)	51(16%)	29(19%)	>0.05
Hemodialysis:	1580(94.4%)	870(93.3%)	295(92.2%)	144(95.4%)	>0.05
Hemodialysis Duration mean±SD	1.72±0.59	1.65±0.47	1.59±0.46	1.49±0.29	>0.05

	Group I 1665 KTRs No. (%)	Group II 932 KTRs No. (%)	Group III 320 KTRs No. (%)	Group IV 151 KTRs No. (%)	P-value
HLA class I mismatch:					
1mismatch	260(15.6%)	132(14.2%)	31(9.7%)	20(13.3%)	
2 mismatch	729(43.8%)	587(63%)	127(39.7%)	55(36.4%)	***<0.05***
3 mismatch	288(17.3%)	97(10.4%)	86(26.9%)	34(22.5%)	
4 mismatch	172(10.3%)	50(5.4%)	50(15.6%)	23(15.2%)	
HLA class II (DR)mismatch:					
1 mismatch	1392(83.6%)	849(91.1%)	286(89.4%)	121(80.1%)	***<0.05***

Kidney transplant recipients (KTRs), Standard Deviation (SD).

P-value <0.05 is statistically significant and >0.05 is statistically non-significant.

Table 2: Immunosuppressive plans:

	Group I 1665 KTRs No. (%)	Group II 932 KTRs No. (%)	Group III 320 KTRs No. (%)	Group IV 151 KTRs No. (%)	P-value
Induction therapy:					
Yes	1052(63.2%)	703(75.4%)	217(67.8%)	130(86.1%)	***<0.05***
No	613(36.8%)	229(24.6%)	103(32.2%)	21(13.9%)	
Type of induction:					***<0.05***
ATG	112(6.7%)	66(7.1%)	44(13.7%)	11(7.3%)	
OKT3	13(0.8%)	0(0%)	2(0.6%)	2(1.3%)	
Basiliximab	892(53.6%)	611(65,6%)	163(50.9%)	111(73.5%)	
Daclizumab	10(0.6%)	9(1%)	1(0.3%)	1(0.7%)	
Campath	25(1.5%)	17(1.8%)	7(2.2%)	5(3.3%)	
Dual therapy	615(36.9%)	284(30.5%)	73(22.8%)	38(25.2%)	***<0.05***
Triple therapy	1050(63.1%)	648(69.5%)	247(77.2%)	113(74.8%)	
Steroid-based	1351(81.1%)	699(75%)	270(84.4%)	116(76.8%)	***<0.05***
Cyclosporine-based	694(41.7%)	354(38%)	168(52.5%)	60(39.7%)	***<0.05***
Tacrolimus-based	732(44%)	520(55.8%)	122(38.1%)	88(58.3%)	***<0.05***
Sirolimus-based	116(7%)	62(6.7%)	28(8.8%)	7(4.6%)	>0.05
Everolimus-based	37(2.2%)	36(3.9%)	5(1.6%)	5(3.3%)	***<0.05***
Mycophenolate-based	719(43.2%)	508(54.5%)	127(39.7%)	86(57%)	***<0.05***
Azathioprine-based	705(42.3%)	313(33.6%)	159(49.7%)	47(31.1%)	***<0.05***

Kidney transplant recipients (KTRs).

P-value <0.05 is statistically significant and >0.05 is statistically non-significant.

Table 3: Rejection and post-transplantation medical complications:

	Group I 1665 KTRs No. (%)	Group II 932 KTRs No. (%)	Group III 320 KTRs No. (%)	Group IV 151 KTRs No. (%)	P-value
Acute rejection:					***<0.05***
No	1161(69.7%)	679(72.9%)	226(70.6%)	120(79.5%)	
Hyper-acute	19(1.1%)	4(0.4%)	1(0.3%)	0(0%)	
Acute cellular	442(26.5%)	224(24%)	77(24.1%)	20(13.2%)	
Vascular	43(2.6%)	25(2.7%)	16(5%)	11(7.3%)	
Acute tubular necrosis	70(4.2%)	54(5.8%)	12(3.8%)	5(3.3%)	>0.05
Chronic rejection	307(18.4%)	139(14.9%)	49(15.3%)	10(6.6%)	***<0.05***
Hypertension	755(45.3%)	382(41%)	187(58.4%)	71(47%)	***<0.05***
Diabetes	217(13%)	59(6.3%)	94(29.4%)	36(23.8%)	***<0.05***

	Group I 1665 KTRs No. (%)	Group II 932 KTRs No. (%)	Group III 320 KTRs No. (%)	Group IV 151 KTRs No. (%)	P-value
Hepatic impairment	155(9.3%)	81(8.7%)	45(14.1%)	19(12.6%)	***<0.05***
Bacterial infection	166(10%)	108(11.6%)	51(15.9%)	28(18.5%)	***<0.05***
Viral infection	122(7.3)	71(7.6%)	30(9.4%)	21(13.9%)	***<0.05***
Malignancy	58(3.5%)	17(1.8%)	25(7.8%)	7(4.6%)	***<0.05***

Kidney transplant recipients (KTRs).
P-value <0.05 is statistically significant and >0.05 is statistically non-significant.

Table 4: Post-transplantation surgical complications:

	Group I 1665 KTRs No. (%)	Group II 932 KTRs No. (%)	Group III 320 KTRs No. (%)	Group IV 151 KTRs No. (%)	P-value
Bleeding					>0.05
Yes	4(0.2%)	2(0.2%)	0(0%)	1(0.7%)	
No	1661(99.8%)	930(99.8%)	320(100%)	150(99.3%)	
Hematomas					>0.05
Yes	5(0.3%)	3(0.3%)	1(0.3%)	0(0%)	
No	1660(99.7%)	929(99.7%)	319(99.7%)	151(100%)	
Lymphocele					***<0.05***
Yes	171(10.3%)	76(8.2%)	45(14.1%)	8(5.3%)	
No	1494(89.7%)	856(91.8%)	275(85.9%)	143(94.7%)	
Wound dehiscence					***<0.05***
Yes	30(1.8%)	11(1.2%)	23(7.2%)	6(4%)	
No	1635(98.2%)	921(98.8%)	297(92.8%)	145(96%)	
Wound infection					***<0.05***
Yes	242(14.5%)	92(9.9%)	50(15.6%)	10(6.6%)	
No	1423(85.5%)	840(90.1%)	270(84.4%)	141(93.4%)	

Kidney transplant recipients (KTRs).
P-value <0.05 is statistically significant and >0.05 is statistically non-significant.

Table 5: Serum creatinine follow-up over 5 years after transplantation:

	Group I 1665 KTRs mean±SD	Group II 932 KTRs mean±SD	Group III 320 KTRs mean±SD	Group IV 151 KTRs mean±SD	P-value
S. cr after 1 year (mg/dl)	1.23±0.67	1.43±0.7	1.27±0.46	1.63±0.39	***<0.05***
S. cr after 2 year (mg/dl)	1.34±0.66	1.56±0.75	1.31±0.48	1.6±0.75	***<0.05***
S. cr after 3 year (mg/dl)	1.47±0.7	1.73±0.6	1.32±0.49	1.81±0.45	***<0.05***
S. cr after 4 year (mg/dl)	1.50±0.70	1.64±0.19	1.38±0.68	1.87±0.75	***<0.05***
S. cr after 5 year (mg/dl)	1.55±0.61	1.80±0.25	1.50±0.68	1.90±0.18	***<0.05***
S. cr at last follow-up (mg/dl)	1.94±0.49	2.38±0.26	2.07±0.26	2.96±0.23	***<0.05***
Creatinine clearance at last follow up (ml/min)	67.20±33.38	66.10±32.82	68.82±34.74	56.70±29.71	***<0.05***

Kidney transplant recipients (KTRs), Standard Deviation (SD), Serum creatinine (S. cr).
P-value <0.05 is statistically significant and >0.05 is statistically non-significant.

Figure (1): Kaplan-Meyer curve illustrating 5, 10, 15 years graft survival in the four groups

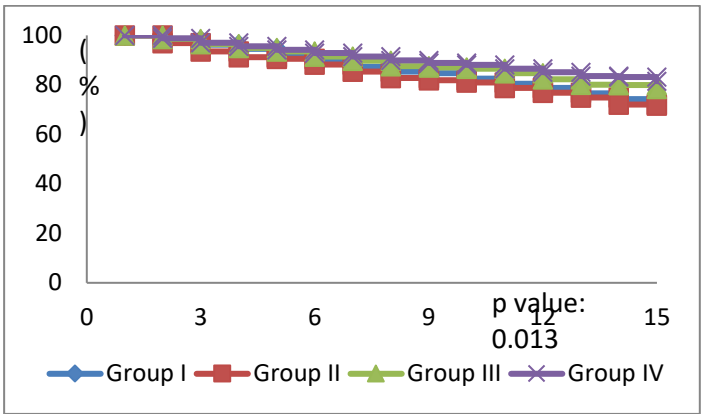
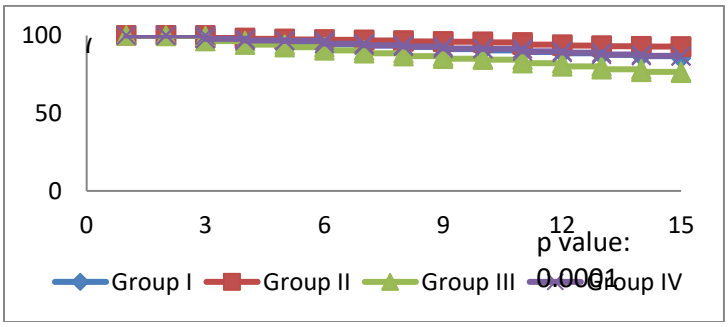


Figure (2): Kaplan-Meyer curve illustrating 5, 10, 15 years patient survival in the four groups



DISCUSSION

The number of elderly patients seeking transplantation is growing, representing the main segment of patients awaiting transplantation (20). Previous reports based on the Scientific Registry of Transplant Recipients database have demonstrated a significant reduction of elderly patients mortality rates after receiving renal transplants compared with staying on dialysis (12) & (21).

When kidney transplantation is considered, age becomes one of the most important factors affecting transplant outcomes. Donors and recipients' different ages combinations have become used recently and reported to have a positive impact on long-term patient and graft survival (14).

In this study, we found that the majority of old donors were females in both young and old recipients groups. This can be explained by that older donors are mostly mothers and wives. As the rule in our center is living-related donor transplantation.

We observed that the incidence of pre-transplant hypertension was higher among old recipients groups with a statistically significant difference (p value: 0.0001). Atherosclerosis and vascular calcification are accused of the high incidence of pre-transplant hypertension in old recipients**.**

With respect to the pre-transplant immunologic work up, most of patients were mismatched in 2 alleles of HLA class I and 1 allele of HLA class II. Overall, we accept in our center up to 5 out of 6 mismatches if the couple is matched in 1 class II allele.

As regards the transplant surgery, ischemia time was shorter in young donors and recipients group and longer in old donors and recipients group with statistical significant difference (p value: 0.0001). Ischemia time was prolonged due to age-related vascular calcifications and atherosclerosis.

As regards immunosuppressive therapy, induction therapy in our center is the role, and determining the type of induction therapy depends on the degree of HLA-mismatch and anti-HLA antibodies titer. As we perform low-risk or moderate-risk transplantation, Basiliximab was the commonly used type of induction in most of our patients.

As regards rejection episodes post-transplantation, we found that the incidence of

acute rejection was less among old recipients from old donors and more among young recipients from young donors with statistically significant difference (p value: 0.0001). Tullius et al., (16) observed decreasing rates of acute rejections with each cohort of increasing recipient age (16). By contrast, The Euro-transplant Senior Program found that elderly recipients receiving kidneys from donors aged ≥65 years had a high rate of rejection (29.1%) regardless of HLA matching (22). Elderly recipients exhibit differences in immune function, including reduced naive T cells (16), increased regulatory T cells (23), impaired function of antigen-presenting cells such as dendritic cells (24), and altered cytokine profiles (25) which made them at higher risk of infections and reduced frequencies of acute rejection (26), while young recipients have relatively high state of immune responsiveness to allo-antigens (27).

The incidence of acute tubular necrosis (ATN) in our study was higher among old donors to young recipients group, with no statistically significant difference. Our result comes in line with Aslam et al., (28) who reported that post-transplant renal complications including ATN was higher in older donors to younger recipients group with statistically significant difference (p value: 0.04) (28). These results can be explained by older donor grafts show a gradual loss of functional nephron mass (29) and limited capacity to respond appropriately to physiologic challenges when transplanted into younger recipients (30).

We observed that the incidence of chronic rejection was higher in young recipients from young donors group and lowest in old recipients from old donors group with statistically significant difference (p value: 0.001). The most important risk factor of chronic rejection is previous acute rejection which is more frequent in group I (30).

In our work, most of the patients in young donors to old recipients group developed post-transplant hypertension with statistically significant difference (p value: 0.0001). Most of the patients in group III were hypertensive before transplantation which is considered one of the most prominent causes of hypertension in renal transplant recipients post-transplantation. In addition, most of the patients in group III were maintained on cyclosporine-based therapy which has been reported to increase the incidence of post-transplant hypertension (31) by increasing the number of angiotensin II type 1 receptors in vascular smooth muscle cells resulting in renal vasoconstriction (32).

The incidence of post-transplant diabetes was higher among old recipients (group III, IV) with statistically significant difference (p value: 0.0001). This result comes in agreement with Gomes et al., (33) who reported that the new-onset diabetes after transplantation (NODAT) cases had mean age of 49.6 ± 10.8 years (33). Older age is the strongest and most consistent risk factor for NODAT in kidney transplantation and is reported in the majority of studies (34).

As regards post-transplant malignancy, the incidence was higher among young donors to old recipients group with statistically significant difference (p value: 0.0001). Old recipients age is considered a risk factor for post-transplant malignancy (35). Most of the recipients in group III were maintained on CSA and azathioprine based immunosuppressive therapy which is associated with high incidence of post-transplant malignancy (36).

As regards post-transplant surgical complications, the incidence of post-transplant lymphocele was higher among young donors to old recipients group with statistically significant difference (p value: 0.004). Ulrich et al., (37) reported that recipients with lymphocele had a significantly higher age (53.3 ± 12.9 vs. 49.7 ± 11.9 years) with statistical significance difference (p value: 0.039) (37). We found that the incidence of wound dehiscence was higher among old recipient groups with statistically significant difference (p value: 0.0001). Old age has been reported as a significant risk factor for post-transplant lymphocele and wound dehiscence due to altered nutritional status leading to impaired tissue healing and prolonged lymphorrhea (38) & (39). The incidence of wound infections was higher among group III including old recipients and group I including young recipients with statistically significant difference (p value: 0.0001). Older adults are at higher risk of post-transplant wound infections due to immunosenescence, frailty, functional impairment and multiple comorbidities (40) also, the incidence of post-transplant diabetes is higher among recipients of group III which is considered as an independent risk factor for post-transplant wound infection (38).

As regards graft survival, we found that

overall 5, 10 and 15 years graft survival was better in old donors to old recipients group and worse in old donors to young recipients group (p value: 0.013). Our results come in agreement with Shin et al., (41) who reported the same results (41) while, Shahani et al., (42) reported that elderly donors kidneys transplanted in elderly recipients had the lowest graft survival as compared to young recipients (80% vs. 75%) and the highest graft survival was in young donors to old recipients group (42). As the physiologic renal reserves of older donors grafts are ultimately lower, to satisfy the metabolic needs and immunologic differences of the recipients, older kidneys are best matched to older recipients (43). In addition, elderly recipients exhibit differences in immune function explaining the lower risk of rejection in older recipients (16).

As regards patient survival, overall 5, 10 and 15 years patient survival was higher in old donors to young recipients group and lower in young donors to old recipients group (p value: 0.0001). Like our results, Tullius et al., (16) reported that Patient survival was age dependent and declined with every cohort of increasing recipient age (16). In our study, incidence of post-transplant HTN, DM and malignancy was the highest in group III and the lowest in group II which certainly affects patient survival after renal transplantation (44) & (36).

Points of strength: we evaluated a large number of patients (3068 KTRs) over a long period of time (about four decades). Our population received different types of induction immunosuppressive protocols and maintenance immunosuppressive protocols. To the best of our knowledge, this is the first study that evaluates the impact of combined age of living donor and recipient of kidney transplantation on patient and graft survival using this large population and over this long period of time.

Study Limitations: Our study had some limitations as it was a single-center experience.

Recommendations: It's recommended that older donors' kidneys should be allocated in older recipients, as this may improve overall graft survival. Older recipients are at lower risk of rejection episodes, so we recommend modulating and decreasing immunosuppressive regimen also to decrease incidence of post-transplant infections and malignancy which are higher in older recipients. Younger recipients are better to be maintained on strong immunosuppressive regimen, as they are at a higher risk of rejection episodes. It is better to avoid allocation of older donors' kidneys in younger recipients, as it may lead to a decrease in the overall graft survival.

CONCLUSION

Combined donor-recipient age affects both graft function and transplantation complications. Young donor to young recipient transplantation was associated with higher incidence of rejection. Old donor to young recipient transplantation was associated with the best patient survival, lower incidence of post-transplant medical complications but the worst graft survival. Young donor to old recipient transplantation was associated with higher incidence of post-transplant medical complications and malignancy and worst patient survival. Old donor to old recipient transplantation was associated with the lowest incidence of rejection and the best graft survival.

Conflict of Interest: Nothing to declare.

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