



OUTCOMES OF RENAL TRANSPLANTATION WITH SIBLING AND SPOUSAL DONORS; A COMPARATIVE STUDY

Dr. M. V. K. Hareesh*

D.M. (Nephrology) Senior Resident, S G P G I, LUCKNOW *Corresponding Author

Dr. R. K. Sharma

Professor of Nephrology, S G P G I, LUCKNOW

ABSTRACT **BACKGROUND:** Kidney transplantation is the best treatment for End stage renal disease. In the recent years due to increase in number of patients requiring transplantation, there is a shortage of donor organs. Spousal transplantation is emerging as an important way of increasing the donor pool. We present a comparison between Spousal donors (SPD) and sibling donors (SID). **METHODS:** 202 renal transplant recipients, 101 with sibling donors and 101 with spousal donors matched for age and sex of donor and year of transplantation were compared. Outcomes like graft and patient survival, early and late graft rejections, infections, post-transplant diabetes mellitus, recurrence of diseases were compared. **RESULTS:** During follow up there is no significant difference between graft and patient survival between the two groups. Graft rejections were more common among the SPD group but were not statistically significant. Recurrences of diseases were more often observed in SID group. The incidence of infections were similar between two groups. **CONCLUSION:** The outcomes of spousal donor (SPD) and sibling donor (SID) transplant recipients were equivalent. An emotionally motivated spousal donor is the solution for the shortage of donor organs as sibling donations are declining in recent years.

KEYWORDS : Kidney transplantation, sibling donors, spousal donors

INTRODUCTION.

Ever since the transplantation of human organs started it has undergone numerous changes. First started the transplantation between identical twins (1). HLA matching has played a key role in determining the donor pool. HLA-DR mismatches are associated with a risk of early graft rejection and graft loss whereas HLA-A, HLA-B antigen mismatches are associated with late graft rejection and loss (2). It has been experienced that recipients of living unrelated donors have better outcomes when compared to cadaveric donors. This led to illegal organ trafficking in many parts of the world including India (3). After the enforcement of Transplantation of Human organs Act 1994 (4), the scenario has changed. Near relatives are the spouses, siblings, parents and children who are 18 yrs of age or older. Special Authorisation committee is required for all other donors. Spouse as donor embodies psychosocial considerations and careful decision making on part of the caregivers. In our centre there has been steady increase in the number of spousal donors over the past 10 years. The number of sibling donors has decreased but the number of parental donors have increased probably due to the decrease in joint family system. A few number of studies were done comparing the donor category and transplant outcomes like between spousal and other related donors, maternal and paternal donors. (5)

MATERIAL AND METHODS

A retrospective cohort study of 202 Living related kidney transplant recipients with sibling or spouse as donor from January 2006 to December 2015 of kidney transplants done at SGPGI, LUCKNOW, were included in the study. Sample included patients in either group who can be matched with a recipient whose donor sex, age were matched and transplanted in the same year. Among them 101 patients had spousal donors and 101 patients had sibling donors. The spousal donor and sibling donor transplant recipients groups were matched for the age and sex of the donor. All were ABO compatible transplantations. The induction and immunosuppression received were comparable between two groups. These patients were followed up till November 2016.

Patients were given immunosuppression with either cyclosporine or tacrolimus combined with Mycophenolate Mofetil and prednisolone. From 2012 all patients received Tacrolimus immunosuppression. The age and sex of the donors were matched while including patients into the study. Choice of induction was based on immunological risk. Second transplants, patients with prior cross match positivites, patients with DSA positivity were given Antithymocyte globulin. Standard protocols were followed for surgery and antibiotic Cotrimoxazole and antifungal prophylaxis with clotrimazole lozenges or mouth paint were given. Empirical Methyl prednisolone was given during postoperative period based on Clinician's discretion for suspected rejection as most early rejections

are mild and responded to methyl prednisolone. Some patients were switched to Everolimus due to biopsy proven CNI toxicity.

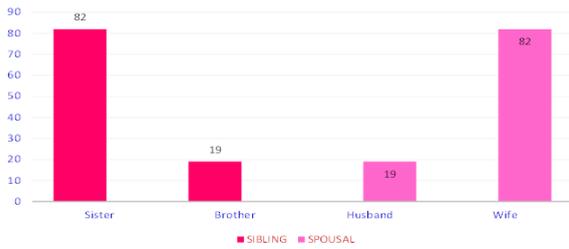
SPSS statistics software version 20 was used for statistical calculations. Kaplan Meier curves were used to compare survival. Death censored graft survival was used for graft survival. Chi-square test was used to compare significance in categorical variables and Independent samples T test was used for non-categorical variables.

BASELINE CHARACTERISTICS

| | SIBLING DONOR GROUP (SID) (n=101) | SPOUSAL DONOR GROUP (SPD) (n=101) | P VALUE |
|------------------------------|-----------------------------------|-----------------------------------|--------------|
| SEX | | | 0.582 |
| MALE | 81(80.2%) | 85(84.2%) | |
| FEMALE | 20(19.8%) | 16(15.8%) | |
| AGE-MEAN(YRS) | 42.86+/-10.46 | 44.97+/-8.14 | >0.05 (1.00) |
| BASIC KIDNEY DISEASE | | | 0.146 |
| CGN | 63(62.4%) | 49(48.5%) | |
| CIN | 21(20.8%) | 36(35.6%) | |
| DKD | 13(12.9%) | 15(14.9%) | |
| RIGHT SOLITARY | 1(1%) | | |
| B/L SCARRED | 1(1%) | | |
| HYPERTENSIVE NEPHROSCLEROSIS | 1(1%) | | |
| ADPKD | | 1(1%) | |
| DGGS | 1(1%) | | |
| COMORBIDITIES | | | |
| D.M. | 14(13.9%) | 15(14.9%) | >0.05 (1.00) |
| CAD | 2(2%) | 5(5%) | 0.248 |
| H/O BLOOD TRANSFUSIONS | 31(30.7%) | 24(23.8%) | 0.343 |
| SECOND TRANSPLANT | 4(4%) | 5(5%) | 0.733 |
| H/O PREGNANCIES | 1(1%) | 7(6.9%) | 0.029 |
| DIALYSIS DURATION (MONTHS) | 9.80+/-7.62 | 9.54+/-7.82 | 0.895 |
| BLOOD GROUP | | | 0.576 |
| A POSITIVE | 19(18.8%) | 22(21.8%) | |
| A NEGATIVE | 1(1%) | 1(1%) | |
| B POSITIVE | 32(31.7%) | 40(39.6%) | |
| AB POSITIVE | 11(10.9%) | 14(13.9%) | |
| AB NEGATIVE | | | |

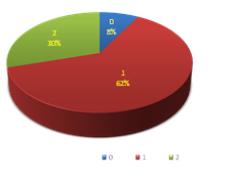
| | | | |
|-------------------|---------------|--------------|--------|
| O POSITIVE | 32(31.7%) | 21(20.8%) | |
| O NEGATIVE | 4(4%) | 2(2%) | |
| Donor relation | | | <0.001 |
| SISTER | 82(40.6%) | | |
| BROTHER | 19(8.8%) | | |
| HUSBAND | | 19(8.8%) | |
| WIFE | | 82(40.6%) | |
| MEAN AGE(YRS) | 40.72+/-10.21 | 41.41+/-9.37 | 0.481 |
| BLOOD GROUP DONOR | | | 0.485 |
| A POSITIVE | 18(17.8%) | 10(9.9%) | |
| A NEGATIVE | | | |
| B POSITIVE | 30(29.7%) | 28(27.7%) | |
| B NEGATIVE | 2(2%) | 1(1%) | |
| AB POSITIVE | 2(2%) | 2(2%) | |
| O POSITIVE | 48(47.5%) | 57(56.4%) | |
| O NEGATIVE | 1(1%) | 3(3%) | |

DONOR RELATION

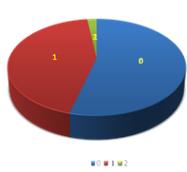


| | | | |
|--------------|---------------------|---------------------|--------|
| HLA DR MATCH | SIBLING DONOR (SID) | SPOUSAL DONOR (SPD) | <0.001 |
| 0 | 8(8.2%) | 53(54.1%) | |
| 1 | 61(62.2%) | 43(43.9%) | |
| 2 | 29(29.6%) | 2(2%) | |
| HLA MATCH | | | <0.001 |
| 0 | 6(6.3%) | 23(24.7%) | |
| 1 | 5(5.3%) | 33(35.5%) | |
| 2 | 9(9.5%) | 19(20.4%) | |
| 3 | 42(43.2%) | 15(16.1%) | |
| 4 | 16(16.8%) | 1(1.1%) | |
| 5 | 11(11.6%) | 2(2.2%) | |
| 6 | 7(7.4%) | 0 | |

HLA MATCH - SIBLING



HLA MATCH - SPOUSAL



RESULTS

A total of 202 kidney transplant recipients were compared. Only the patients with sibling donors or spousal donors were chosen for analysis and matched for the age and sex of the donor and length of the follow up period. Among the recipients of sibling donors, 80.2% (n=81) were males and 19.8% (n=20) were females whereas in spousal donor group 84.2% (n=85) were males and 15.8% (n=16) were females. There was no significant difference in the male and female distribution between the two groups (p=0.582). The recipients of the SPD group were slightly older than the recipients of the SID group (mean age +/- Standard deviation 44.97 +/- 8.14 yrs Vs 42.86 +/- 10.46 yrs, p>0.05).

There was difference in the basic disease of the recipient in the two groups. Chronic glomerulonephritis was the commonest but the proportion was more in the SID group (62.4%) than the SPD group (48.5%), whereas the percentage of Chronic interstitial nephritis was more in SPD group than the SID group (35.6% vs 20.8%). Diabetic kidney disease was nearly equal in both (SID 12.9% (n=13) vs SPD 14.9% (n=15)).

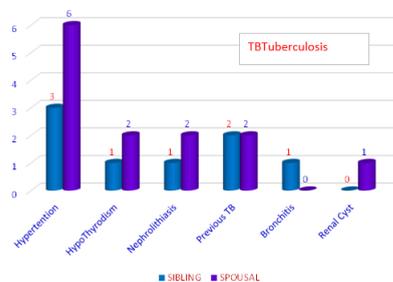
More recipients in the SID group received blood transfusions compared to the SPD group (30.7% vs 20.8%) (p=0.343). More recipients in the SPD group had previous pregnancies compared to SID group (6.9%, n=7 vs 1%, n=1) (p=0.029). DSA positivity was observed in

4% of recipients in SPD group compared to none in SID group. Flow cytometry cross match positivity was seen in 3% of patients in SID group and 5% of patients in SPD group.

| IMMUNOLOGICAL PARAMETERS | SIBLING DONOR GROUP (SID) | SPOUSAL DONOR GROUP (SPD) | P Value |
|-------------------------------------|---------------------------|---------------------------|---------|
| FIRST CROSS MATCH POSITIVITY | 3(3%) | 1(1%) | 0.312 |
| FINAL CROSS MATCH POSITIVITY | 2(2%) | 2(2%) | >0.05 |
| DSA NOT AVAILABLE | 83(82.2%) | 81(80.2%) | 0.247 |
| DSA CLASS 2 POSITIVE | | 3(3%) | |
| DSA CLASS 1,2 POSITIVE | | 1(1%) | |
| NEGATIVE DSA | | | |
| FLOW CYTOMETRY | | | 0.518 |
| NOT AVAILABLE | 85 | 84 | |
| NEGATIVE | 13 | 12 | |
| T CELL CROSSMATCH POSITIVE | 3(3%) | 2(2%) | |
| B CELL CROSSMATCH POSITIVE | 0 | 1(1%) | |
| BOTH B & T CELL CROSSMATCH POSITIVE | 0 | 2(2%) | |

| DONOR CHARACTERISTICS | SIBLING DONOR GROUP (SID) | SPOUSAL DONOR GROUP (SPD) | P VALUE- |
|---------------------------------------|---------------------------|---------------------------|----------|
| DONOR COMORBIDITIES | | | 0.439 |
| HYPERTENSION | 3(3%) | 6(6%) | |
| HYPOTHYROIDISM | 1(1%) | 2(2%) | |
| RENAL STONE | 1(1%) | 2(2%) | |
| PREVIOUS TB | 2(2%) | 2(2%) | |
| BRONCHITIS | 1(1%) | | |
| RENAL CYST | | 1(1%) | |
| NO COMORBIDITY | 91(91%) | 84(84%) | |
| GFR | | | |
| TOTAL MEAN GFR | 85.31 +/- 16.45 | 84.09 +/- 15.59 | 0.773 |
| GFR OF TRANSPLANTED KIDNEY | 42.29 +/- 8.67 | 41.86 +/- 7.91 | 0.771 |
| PREVIOUS SURGERIES | 24(23.9%) | 31(31%) | 0.160 |
| SURGERY CHARACTERISTICS | | | |
| MULTIPLE VESSELS | 16(15.8%) | 17(16.8%) | >0.05 |
| DIFFICULT SURGERY | | 2(2%) | 0.155 |
| POST OPERATIVE ACUTE TUBULAR NECROSIS | 7(6.9%) | 3(3%) | 0.206 |
| IMMUNOSUPPRESSION | | | 0.546 |
| TACROLIMUS | 65(64.4%) | 70(69.3%) | |
| CYCLOSPORINE | 35(34.7%) | 30(29.7%) | |
| CHANGE TO EVEROLIMUS | 4(4%) | 2(2%) | 0.407 |
| INDUCTION | | | 0.917 |
| ATG | 8(7.9%) | 10(9.9%) | |
| BASILIXIMAB | 41(40.6%) | 39(38.6%) | |
| DACLIZUMAB | 2(2%) | 3(3%) | |
| NO INDUCTION | 49(48.5%) | 47(46.5%) | |

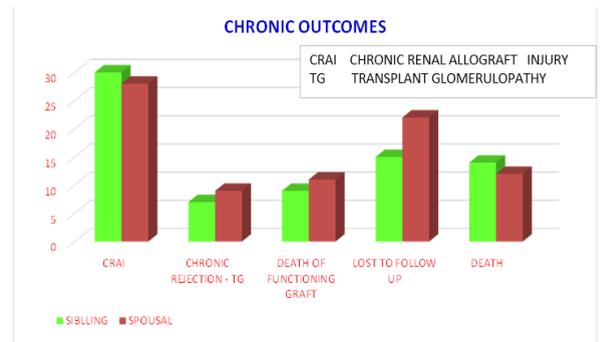
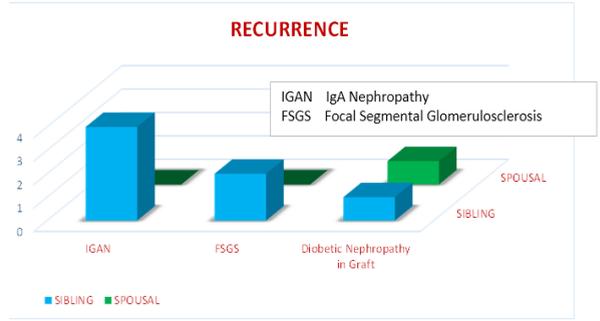
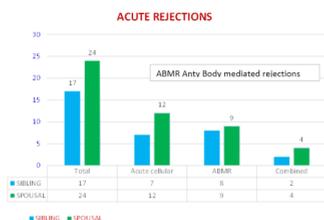
DONOR COMORBIDITIES



In the SID group, 82 were sisters and 19 were brothers whereas in SPD group, 82 were wives and 19 were husbands. The mean age of donors in both the groups was 40.72 and 41.41 yrs respectively. The comorbidities and mean GFR between the two groups was similar (85.31±16.45ml/mt Vs 84.09±15.59ml/mt). The total degree of HLA match and HLA DR match was significantly more in SID group than the SPD group (p<0.01). The percentage of donors with previous surgeries were comparable between these two groups. (23.9% vs 31%,p=0.16). Percentage of grafts with multiple vessels was also comparable (15.8% vs 16.8%).

There was no significant difference in the proportion of recipients who received induction in the SID group compared with SPD group (SID,n=49,51.5%;SPD,n=47,53.5%;p=0.917). The proportion of patients who received Antithymocyte globulin (SID(7.9%) vs SPD(9.9%)) and basiliximab (SID 40.6% vs SPD 38.6%) as induction was also similar. There was no difference in the proportion of patients with Tacrolimus immunosuppression (SID,64.4% Vs SPD 69.3%,p=0.546) in between two groups. Four patients were changed from CNi to Everolimus immunosuppression in SID group when compared to two in SPD group.

| OUTCOMES | | | |
|--------------------------------|-------------|-------------|-------|
| STEROID PULSE | 15(14.9%) | 17(16.8%) | 0.230 |
| HOSPITAL STAY | | | |
| ATG SECONDARY | 1(1%) | 5(5%) | |
| RESPONSE TO STEROID PULSE | 11(10.9%) | 13(12.9%) | |
| DURATION HOSPITAL | 23.44±11.47 | 24.5±13.10 | 0.615 |
| EARLY BIOPSY PROVEN REJECTIONS | 11(10.9%) | 16(15.8%) | 0.409 |
| LATE REJECTIONS | 6(5.9%) | 9(8.9%) | 0.593 |
| TOTAL ACUTE REJECTIONS | 17(16.8%) | 24(23.7%) | 0.502 |
| REJECTION TYPE | | | 0.486 |
| ACR | 7(6.9%) | 12(11.9%) | |
| ABMR | 8(7.9%) | 9(8.9%) | |
| COMBINED | 2(2%) | 4(4%) | |
| TREATMENT RECEIVED | | | |
| IV MP | 5(5%) | 4(4%) | |
| IVMP ,ATG | 2(2%) | 1(1%) | |
| ATG | 4(4%) | 8(7.9%) | |
| IVMP+PP+IVIG | 1(1%) | 0 | |
| PP+IVIG+ATG | 1(1%) | 2(2%) | |
| BORTEZOMIB | 0 | 1(1%) | |
| ATG+IVIG | 0 | 1(1%) | |
| PP+IV IG | 1(1%) | 4(4%) | |
| PP+IV IG+RITUXIMAB | 0 | 1(1%) | |
| NO TREATMENT GIVEN | 2(2%) | 1(1%) | |
| TREATMENT RESISTANT REJECTIONS | 1(1%) | 7(6.9%) | 0.058 |
| RECURRENCE | | | |
| IGAN | 4 | 0 | |
| FSGS | 2 | 0 | |
| DIABETIC NEPHROPATHY GRAFT | 1 | 1 | |
| NODAT | 25(24.8%) | 19(18.8%) | 0.394 |
| DEATH | 14(13.9%) | 12(11.9%) | 0.834 |
| CRAI | 30(29.7%) | 28(27.7%) | 0.876 |
| CHRONIC REJECTION-TG | 7(6.9%) | 9(8.9%) | 0.795 |
| DEATH FUNCTIONING GRAFT | 9(8.9%) | 11(10.9%) | 0.814 |
| LOST TO FOLLOW UP | 15(14.9%) | 22(21.8%) | |
| GRAFT SURVIVAL MEAN | 58.87±37.49 | 50.95±38.85 | 0.205 |
| PATIENT SURVIVAL MEAN | 59.36±37.68 | 53.30±39.61 | 0.260 |



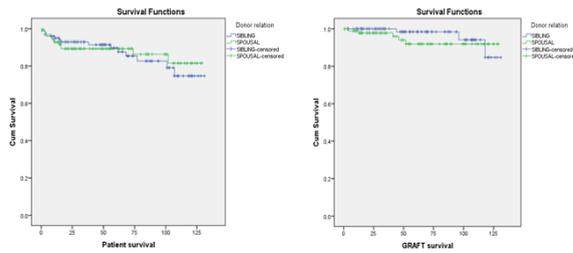
There were 11 biopsy proven early rejections in the SID group when compared to 16 in the SPD group (p=0.409). Number of late rejections were also more in the SPD group (9) compared to SID group (6)(p=0.593). Acute cellular rejections were more in the SPD group compared to SID group (6.9%,n=7, Vs 11.9%,n=12). Resistant rejections were more common in the SPD group compared to SID group (n=7 Vs n=1;p=0.058). 5 patients in the SPD group required ATG for the treatment of Steroid resistant rejection whereas only one pt required it in SID group.

The incidence of PTDM was more in the SID group (24.8% Vs 18.8%) but was not statistically significant (p=0.354). Biopsy proven recurrence of basic diseases was more common in SID group with recurrence noted in 7 patients out of which 4 were IgA Nephropathy, 2 were FSGS, 1 was Diabetic Nephropathy. Only one case of recurrence was noted in spousal group diabetic nephropathy

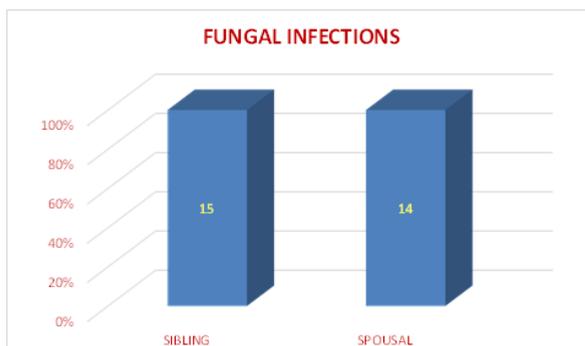
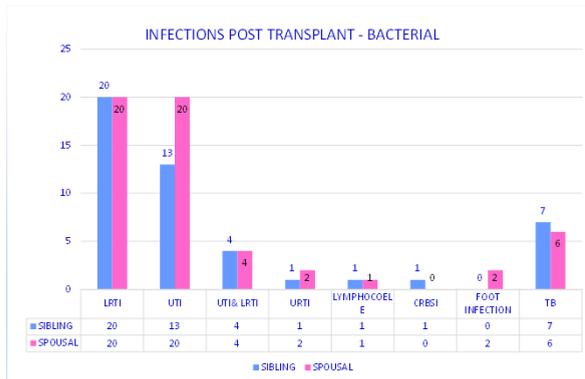
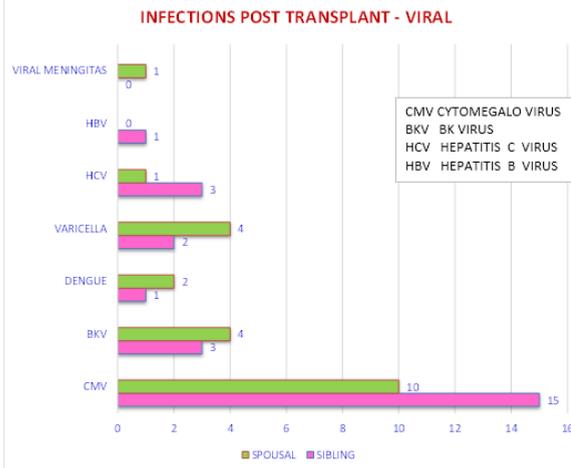
| INFECTIONS | | | |
|--------------------|--------------------|--------------------------|-------|
| CMV | 15(14.9%) | 10(9.9%) | 0.393 |
| BKV | 3(3%) | 4(4%) | 0.710 |
| FUNGAL INFECTIONS | 15(14.9%) | 14(13.9%) | >0.05 |
| LRTI | 20(19.8%) | 20(19.8%) | |
| UTI | 13(12.9%) | 20(19.8%) | |
| UTI,LRTI | 4(4%) | 4(4%) | |
| URTI | 1(1%) | 2(2%) | |
| LYMPHOCOELE | 1(1%) | 1(1%) | |
| CRBSI | 1(1%) | 0 | |
| FOOT INFECTION | 0 | 2(2%) | |
| OTHER BACTERIAL | 16(15.8%) | 7(6.9%) | |
| TB | 7(6.9%) | 6(5.9%) | 0.584 |
| VIRAL | | | 0.549 |
| DENGUE | 1(1%) | 2(2%) | |
| VARICELLA | 2(2%) | 4(4%) | |
| HCV | 3(3%) | 1(1%) | |
| HBV | 1(1%) | 0 | |
| VIRAL MENINGITIS | 0 | 1(1%) | |
| MALIGNANCY | | | 0.591 |
| MALIGNANCY POST TX | 1 MULTIPLE MYELOMA | 1 HEPATOCELLAR CARCINOMA | |

Bacterial, fungal and viral infections were similar between two groups except CMV disease which is more common in SID group compared to SPD group (14.9%,n=15 Vs 9.9%,n=10;p=0.393). Incidence of post-transplant Malignancies was similar, one patient in SID group developed Multiple Myeloma and one patient in SPD group developed Hepatocellular carcinoma.

Kaplan meier curves showing patient and graft survival rates of Sibling donor (SID) and Spousal donor (SPD) transplant recipients



Graft survival rate was less in SPD group compared to SID group in Kaplan Meier survival curve but there was no significant difference in patient survival. Five year graft survival rates were 98% and 92% respectively.



| Pt survival rates | 1yr | 3yr | 5yr | 7yr | 10yr |
|-------------------|-----|-----|-----|-----|------|
| Sibling Donor | 95% | 93% | 90% | 83% | 74% |
| Spousal Donor | 93% | 89% | 89% | 86% | 82% |

| Graft survival rates | 1yr | 3yr | 5yr | 7yr | 10yr |
|----------------------|------|-----|-----|-----|------|
| Sibling Donor | 100% | 98% | 98% | 98% | 86% |
| Spousal donor | 99% | 94% | 92% | 92% | 92% |

Using Spearman's correlation coefficient it was found that graft survival in our study was significantly correlated to HLA matching ,hospital stay duration and CRAI.

| DEATHS | 6 | 6 |
|------------------------------------|-------|-------|
| CAUSE OF DEATH | | |
| LRTI SEPSIS SEPTIC SHOCK | 5(5%) | 5(5%) |
| PYELONEPHRITIS SEPSIS SEPTIC SHOCK | 1(1%) | 0 |
| DENGUE SHOCK SYNDROME | | 1(1%) |

Six deaths occurred in either group,out of which 5 were due to Lower respiratory tract infection severe sepsis and shock.

Graft loss progressing to ESRD was observed in 3 patients in the SID group and 5 patients in the SPD group.

| GRAFT LOSS | | |
|-------------------------------|-------|-------|
| GRAFT LOSS-ESRD | 3(3%) | 5(5%) |
| GRAFT LOSS CAUSE | | |
| BK VIRUS NEPHROPATHY | 1 | |
| VIRAL CYTOPATHIC CHANGES-CRAI | 1 | |
| RECURRENT FSGS | 1 | |
| CRAI -LRTI | | 1 |
| HYDRONEPHROSIS | | 1 |
| RECURRENT HUS-REJECTION | | 1 |
| CRAI-UROSEPSIS | | 1 |
| PYONEPHROSIS-NEPHRECTOMY | | 1 |

DISCUSSION

Kidney transplants have been done with biologically unrelated donors in different parts of the world. This was unregulated in many parts of the world including India resulting in organ trade and clandestine transplantation surgeries. The situation changed in India after the Transplantation of Human Organs Act, 1994(4) was passed. This act defines near relative as spouse, son, daughter, father, mother, brother or sister. Recently the Transplantation of Human Organs and Tissues rules, 2014 dictates the guidelines for Living and cadaveric Kidney donation. Living unrelated donor renal transplantation is not routinely performed in our centre but spousal renal transplantation is performed in our centre. Spouses who have completed at least 3 years of marriage are accepted as donors. Donation is also accepted if consummation of marriage has occurred. Similar policy has been followed in AIIMS, New Delhi (6,7). In united kingdom uses ULTRA for assessment of issues related to genetically unrelated donor. (8)

The number of sibling donors decreased over the years(6). There is a steady increase in the number of spousal donors in the recent years in different centres in India (9) and all over the world(10). Spousal donation embodies emotional attachment between spouses and ensures better compliance with immunosuppression and follow up. Family psychodynamics ,sexual relationship and relationship with children improves with spousal donation(11-13). Spouse as donor comparable to the parental donor and better than the cadaveric donor advocated by Terasaki 1995(1). It also ensures quicker decision, easy coordination(12) when compared to sibling donors.

The immunological matching between donor and recipient using HLA compares with that of the Matter et al Fuller et al Humar et al(14-16). The immunosuppressive protocols were almost similar between the two groups in terms of Induction and Maintenance immunosuppression. Most patients received Cyclosporine as immunosuppression before 2009 which changed to Tacrolimus during 2009-2010 period and completely replaced by Tacrolimus in the years after. This was taken care by selecting the recipients from the same year so that there was no significant difference between the two groups.

In previous studies of Matter et al(14) there was significant donor age difference of the between genetically unrelated donors. Noppakun et al study(17) concluded that the Donor's age influences the transplant outcomes. Our present study has age matched groups eliminating the bias.

The graft survival rates and the patient survival rates were similar between the two groups. (89% vs 90%) similar to Tang et al , Gjertson et al , Yoon et al (18-20). Mukharjee et al Kute et al (21,22) reported similar graft survival rates but statistically significant difference in patient survival between spousal and related donor groups. Biopsy proven early rejections were more common in the spousal donor

group(15.8%) compared to the sibling group (10.9%) but not statistically significant similar to Tang et al Mukharjee et al.(18,21)..This contrasts to the Matter YE et al, Fuller et al, and Matas AJ et al(14,15) where there were statistically significant high incidence of acute rejections in spousal donor group(23).

LIMITATIONS

The main limitation of the present study is 15% -20% of the recipients lost to follow up and the sample size is less(n=101) in each group but matched to the age and sex of donor and year of transplant to ensure comparability between the groups.ABO incompatible transplants were not included in the present study.

CONCLUSION

Spouse as a kidney donor is an ethically viable option in this era where there are unwilling siblings and unfit parents.

REFERENCES

1. Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. *N Engl J Med.* 1995 Aug 10;333(6):333-6.
2. Takemoto S, Port FK, Claas FHI, Duquesnoy RJ. HLA matching for kidney transplantation. *Hum Immunol.* 2004 Dec;65(12):1489-505.
3. Chugh KS, Jha V. Commerce in transplantation in Third World countries. *Kidney Int.* 1996 May;49(5):1181-6.
4. Nundy S. Origin and genesis of the Transplantation of Human Organs Act, 1994, of India. *Int Dig Health Legis.* 1996;47(1):88-90.
5. Lim WH, McDonald SP, Coates PT, Chapman JR, Russ GR, Wong G. Maternal compared with paternal donor kidneys are associated with poorer graft outcomes after kidney transplantation. *Kidney Int.* 2016 Mar;89(3):659-65.
6. Bhowmik D, Dash SC, Tiwari SC, Agarwal SK, Gupta S, Guleria S, et al. Spousal renal donor transplants in India. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* 1999 Aug;14(8):2052-3.
7. Dash SC, Bhowmik D. The wife as kidney donor: current Indian scenario. *Kidney Int.* 2001 Feb;59(2):801.
8. Mathieson PW, Jolliffe D, Jolliffe R, Dudley CR, Hamilton K, Lear PA. The spouse as a kidney donor: ethically sound? *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* 1999 Jan;14(1):46-8.
9. Sakhuja V, Kumar V. Spouses as kidney donors in India: Trends and outcomes. *Indian J Nephrol.* 2014 Jan;24(1):1-2.
10. Chung BH, Jung MH, Bae SH, Kang SH, Hwang HS, Hyoung BJ, et al. Changing Donor Source Pattern for Kidney Transplantation over 40 Years: A Single-Center Experience. *Korean J Intern Med.* 2010 Sep;25(3):288-93.
11. Watanabe T, Hiraga S. Influence on family psychodynamics on spousal kidney transplantation. *Transplant Proc.* 2002 Jun;34(4):1145-7.
12. Binet I, Bock AH, Vogelbach P, Gasser T, Kiss A, Brunner F, et al. Outcome in emotionally related living kidney donor transplantation. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* 1997 Sep;12(9):1940-8.
13. Spital A. Do U.S. transplant centers encourage emotionally related kidney donation? *Transplantation.* 1996 Feb 15;61(3):374-7.
14. Matter YE, Nagib AM, Lotfy OE, Alsayed AM, Donia AF, Refaie AF, et al. Impact of Donor Source on the Outcome of Live Donor Kidney Transplantation: A Single Center Experience. *Nephro-Urol Mon.* 2016 May;8(3):e34770.
15. Fuller TF, Feng S, Brennan TV, Tomlanovich S, Bostrom A, Freise CE. Increased rejection in living unrelated versus living related kidney transplants does not affect short-term function and survival. *Transplantation.* 2004 Oct 15;78(7):1030-5.
16. Living Unrelated Donors in Kidney Transplants: Better Long-Term Results Than With Non-Hla-Identical Living Related Donors? [Internet]. *PubMed Journals.* [cited 2017 Feb 24]. Available from: <https://ncbi.nlm.nih.gov/labs/articles/10830235/>
17. Noppakun K, Cosio FG, Dean PG, Taler SJ, Wauters R, Grande JP. Living donor age and kidney transplant outcomes. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg.* 2011 Jun;11(6):1279-86.
18. Tang S, Lui SL, Lo CY, Lo WK, Cheng IKP, Lai KN, et al. Spousal renal donor transplantation in Chinese subjects: a 10 year experience from a single centre. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* 2004 Jan;19(1):203-6.
19. Gjertson DW, Cecka JM. Living unrelated donor kidney transplantation. *Kidney Int.* 2000 Aug;58(2):491-9.
20. Yoon HE, Song JC, Hyoung BJ, Hwang HS, Lee SY, Jeon YJ, et al. Comparison of long-term outcomes between spousal transplants and other living unrelated donor transplants: single-center experience. *Nephron Clin Pract.* 2009;113(4):c241-249.
21. Mukherjee A, Kekre NS, Gopalakrishnan G. The spouse as a donor in renal transplants. *Saudi J Kidney Dis Transplant Off Publ Saudi Cent Organ Transplant Saudi Arab.* 2006 Mar;17(1):77-81.
22. Kute VB, Shah PR, Vanikar AV, Gumber MR, Goplani KR, Patel HV, et al. Long-term outcomes of renal transplants from spousal and living-related and other living-unrelated donors: a single center experience. *J Assoc Physicians India.* 2012 Jul;60:24-7.
23. Matas AJ, Payne WD, Sutherland DER, Humar A, Gruessner RWG, Kandaswamy R, et al. 2,500 Living Donor Kidney Transplants: A Single-Center Experience. *Ann Surg.* 2001 Aug;234(2):149-64.