

Renal Transplant Outcomes in Spousal and Living-Related Donors in Malaysia

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Abstract

Introduction: Studies have shown that a compatible human leukocyte antigen (HLA) match can confer a favourable effect on graft outcomes. We examined the outcomes of HLA matching in renal transplant donors in Malaysia. **Materials and Methods:** A total of 140 patients who had compatible ABO blood type with negative T-cell lymphocytotoxicity crossmatch were included in the study and 25% of them were spousal transplant donors. No remarkable differences in acute rejection rate, graft survival, patient survival and serum creatinine level were observed between the spousal and living-related donor groups. **Results:** The spousal donor group had a higher degree of HLA mismatch than the living-related donor group. HLA-A mismatch was associated with increased rejection risk at 6 months (odds ratio [OR], 2.75; $P = 0.04$), 1 year (OR, 2.54; $P = 0.03$) and 3 years (OR, 3.69; $P = 0.001$). It was also observed in the deleterious effects of HLA-B and HLA-DQ loci when the number of antigen mismatches increased. The risk was 7 times higher in patients with ≥ 1 mismatch at HLA-A, HLA-B and HLA-DR loci than those who did not have a mismatch at these loci at 6 months ($P = 0.01$), 1 year ($P = 0.03$) and 3 years ($P = 0.003$). **Conclusion:** A good match for HLA-A, HLA-B, HLA-DR and HLA-DQ can prevent acute rejection risk in renal transplant patients. Consequently, spousal donor transplants could be a safe intervention in renal patients.

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Key words: Graft survival, Human leukocyte antigen incompatibility, Immunosuppressant, Patient survival

Introduction

Renal transplantation has substantial benefits for patients with end-stage renal disease (ESRD). Not only is it cost-effective in the long run, it also confers better patient survival and quality of life compared to dialysis treatment.¹ However, the success of any transplantation programme is highly dependent on availability of donors,² accessibility to infrastructure and trained personnel, technological advances in histocompatibility tests,³ use of potent immunosuppressants⁴ and sound health policy.⁵

Generally, living donor kidney transplants (LDKTs) have better outcomes than deceased donor kidney transplants and have been attributed to factors such as higher quality of initial renal function and shorter cold ischaemic time of the organ.⁶ According to the International Registry of Organ Donation and Transplantation, countries that have legislated “presumed consent” on organ donation include Belgium, France, Italy and Spain. Since every resident in these countries is considered a donor, they consistently ranked among states with the highest number of donors worldwide.⁷

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Malaysia, on the other hand, has an “opt in” legislation on organ donation and her residents are required to provide informed consent to donate various organs and tissues in the event of sudden and untimely demise.⁸ Although the country’s living donor transplant policy stipulates that organ donation from emotionally or genetically related donors is acceptable, the number of organ donations in the country remain low. Moreover, any donation by unrelated living donors (except for spousal transplants) must be approved by the Unrelated Transplant Approval Committee and only when no suitable cadaver and related donors are available.⁹

In its 11th report, the National Transplant Registry of Malaysia reported that the number of kidney transplants in the country had declined from 6 individuals in 2005/2006 to 3 individuals in 2014 in 1 million residents.¹⁰ As more Malaysians head overseas for a kidney transplant, the number of dialysis cases in the country doubled in the last 10 years,¹¹ reflecting a growing need for donors. Current legislations on organ donation in Malaysia would only widen the gap between the number of available donors and patients who are awaiting a kidney transplant.¹²

In its 13th report, the National Transplant Registry¹³ reported an increase in the number of living donor transplants in 2016 and approximately half of them were LDKTs. However, they involved mostly living donors who were genetically related and only 7.4% were spousal donors. On the other hand, the rate of cadaveric local transplantations continued to fluctuate through the years and accounted for only 11% of all transplants performed in 2016.

These findings have prompted Malaysia to promote living donor transplants including spousal transplants. Since she has a multiracial population comprising Malays (68.6%), Chinese (23.4%), Indians (7%) and other ethnicities (1%),¹⁴ inter-racial marriages are common and have a recognisable effect in the distribution of human leukocyte antigen (HLA) alleles among her residents. Consequently, spousal donor transplants can predispose patients to increased rejection risk when there is greater HLA disparity between donors and patients.

In the literature, there is a dearth of reports on the degree and impact of HLA disparity on the outcome of spousal donor transplants in Malaysia. A crucial question that must be addressed is whether such transplants can be considered a safe option to improve patients’ eligibility for organ transplantation in the country. To address this issue, in this study we compared the long-term outcomes of spousal and other living-related kidney transplants and examined the clinical relevance of HLA mismatch in patients.

Materials and Methods

The records of 146 patients who received their first renal allograft between March 1996 and April 2014 at

the University Malaya Medical Centre (UMMC) were retrieved and retrospectively reviewed. Thirty-two patients were spousal donor transplants and 109 were living-related donor transplants. Five cases of living non-related donor transplants were excluded due to lack of data. Recipients of combined transplants and paediatric patients were also excluded from this study.

The immunosuppression regimen included triple immunosuppressants of either cyclosporine, mycophenolate acid and steroid or mycophenolate acid, steroid and tacrolimus. According to the transplant protocol of UMMC, cyclosporine (Neoral[®]) was administered at a starting dose of 4–6 mg/kg/day and titrated at 150 ng/mL and 300 ng/mL for 3 months based on trough concentrations, and then at approximately 150 ng/mL thereafter. For tacrolimus (Prograf[®]), the initial dose was 0.2 mg/kg/day and it was titrated at 8–15 ng/mL based on its trough levels in the first 3 months, 5–12 ng/mL in the first year and 5–10 ng/mL thereafter.

All donors and patients had the same blood type—ABO blood group—and had tested negative for T-cell lymphocytotoxicity crossmatch. HLA typing was performed with polymerase chain reaction–sequence-specific oligonucleotide technique or serology. Since the introduction of the transplantation programme in UMMC, HLA class I typing was performed routinely; HLA class II typing was commenced for HLA-DR and HLA-DQ in 2002 and 2006, respectively. When needed, HLA antibodies were detected by serology and solid-phase assay (Luminex[®]).

The number of antigen mismatch for HLA-A, HLA-B, HLA-Cw, HLA-DQ and HLA-DR was defined as the number of donor HLA that differed from those in recipients according to the guidelines on HLA values and split equivalences of the Organ Procurement and Transplantation Network.¹⁵ Graft failures included death of patient and resumption of dialysis; graft rejection was diagnosed based on clinical presentation and/or biopsies. Biopsies were performed to detect early graft rejection and when patients experienced altered graft function that suggested acute rejection. Data on rejection types—such as antibody-mediated, cellular, glomerular or vascular—was not available.

Statistical analysis was performed using SPSS Statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA) to compare baseline characteristics and HLA mismatch between donors and recipients. Graft rejection and continuous variables were analysed using chi-square test and student’s t-tests, respectively. Predictors of acute rejection were modelled by binomial logistic regression. Results were expressed as odds ratio (OR) and 95% confidence interval (CI). A value of $P < 0.05$ was considered statistically significant. This study was approved by UMMC Ethics Committee in accordance with the Helsinki Declaration.

Results

The baseline characteristics of donors and graft recipients are shown in Table 1. In spousal donor grafts, the mean age of graft recipients and donors were 38.48 ± 13.85 years and 32.47 ± 15.45 years, respectively; in living-related donor grafts, it was 33.16 ± 12.48 years and 42.87 ± 15.96 years, respectively. Spousal donors were younger than donors in living-related grafts, but the age difference was not statistically significant ($P = 0.54$).

There were more female donors in living-related grafts than spousal grafts (61% vs 23%, $P > 0.37$), but more men were transplant recipients in spousal grafts than living-related grafts (75% vs 25%, $P = 0.39$). The distribution of Malays, Chinese and Indians was similar in both spousal donor and living-related donor grafts (65%, 19% and 12% vs 67%, 15% and 16%, respectively; $P = 0.74$). All patients were on triple immunosuppressants and medication types were similar in both groups ($P = 0.74$); most patients were on cyclosporine, mycophenolate acid and steroid or mycophenolate acid, steroid and tacrolimus.

The main aetiologies of ESRD in spousal and living-related donors were bilateral small kidneys, hypertensive

nephropathy and immunoglobulin A nephropathy (Table 2); >60% of renal failure was attributed to these diseases. No mortality was reported at 3 years post-transplantation. At 6 months, all 33 transplant recipients in the spousal donor group were well but 2 of the 109 transplant recipients in the living-related donor group had resumed dialysis (100% vs 98%, $P = 0.44$). At 1 year post-transplantation, 3 recipients in each group required dialyses (91% vs 97%, $P = 0.10$); at 3 years post-transplantation, 4 and 7 recipients in both groups, respectively, were on dialysis (Fig. 1). In our study, graft survival in the spousal donor group was comparable to the living-related donor group (88% vs 94%, $P = 0.26$).

At 1 year and 3 years post-transplantation, 8 and 12 patients in the spousal donor group experienced at least 1 acute rejection episode, respectively. At 1 year post-transplantation, 3 and 6 rejection episodes were observed in husband-to-wife and wife-to-husband transplantations, respectively. The rejection rates in the spousal donor group were not higher than the living-related donor group at 6 months (22% vs 18%, $P = 0.66$), 1 year (25% vs 22%, $P = 0.72$) and 3 years (38% vs 39%, $P = 0.84$) (Fig. 2).

Table 1. Baseline Characteristics of Spousal and Living-Related Renal Donors and Recipients Between March 1996 and April 2014

Variable	Spouse (n = 32)	Living-Related (n = 109)	P Value
Age at transplant (mean $\pm$ SD, years)			
Recipient	38.48 ± 13.85	33.16 ± 12.48	0.30
Donor	32.47 ± 15.45	42.87 ± 15.96	0.54
Recipient gender (%)			0.39
Male	24 (75)	73 (25)	
Female	8 (25)	36 (18)	
Donor gender (%)			0.37
Male	8 (16)	41 (39)	
Female	19 (23)	64 (61)	
Ethnicity (donor and recipient, %)			0.74
Chinese	21 (65)	73 (67)	
Indian	4 (12)	18 (16)	
Malay	6 (19)	17 (15)	
Immunosuppressant (%)			0.74
Cyclosporine, mycophenolate acid	6 (19)	15 (14)	
Tacrolimus, mycophenolate acid	21 (66)	73 (67)	
Cyclosporine, mycophenolate mofetil	2 (6)	10 (9)	
Tacrolimus, mycophenolate mofetil	1 (3)	1 (1)	
Cyclosporine, azathioprine	2 (6)	6 (5)	
Tacrolimus, azathioprine	0 (0)	4 (4)	

SD: Standard deviation

Table 2. Clinical Outcomes in Spousal and Living-Related Renal Donors

Variable	Spouse (n = 32)	Living-Related (n = 109)	P Value
Aetiology of ESRD (%)			0.48
Hypertensive nephropathy	7 (21)	27 (25)	
Diabetic nephropathy	3 (9)	10 (9)	
Glomerulonephritis	4 (12)	17 (15)	
Bilateral small kidneys	8 (24)	22 (20)	
Idiopathy	2 (6)	11 (10)	
IgA nephropathy	6 (18)	7 (6)	
Polycystic kidney disease	2 (6)	4 (5)	
Others	1 (3)	11 (10)	
Graft survival (%)			
6 months	32 (100)	107 (98)	0.44
1 year	29 (91)	106 (97)	0.10
3 years	28 (88)	102 (94)	0.26
Acute rejection (%)			
6 months	7 (22)	20 (18)	0.66
1 year	8 (25)	24 (22)	0.72
3 years	12 (38)	43 (39)	0.84
Creatinine level (mean $\pm$ SD, μ mol/L)			
1 month	121.9 $\pm$ 58.50	198.6 $\pm$ 26.50	0.238
6 months	116.38 $\pm$ 17.72	148.28 $\pm$ 8.03	0.108
1 year	108.00 $\pm$ 13.61	137.85 $\pm$ 6.16	0.052
3 years	112.88 $\pm$ 13.19	139.39 $\pm$ 5.98	0.074

ESRD: End-stage renal disease; IgA: Immunoglobulin A; SD: Standard deviation

Note: There is no mortality at 6 months, 1 year and 3 years post-transplantation.

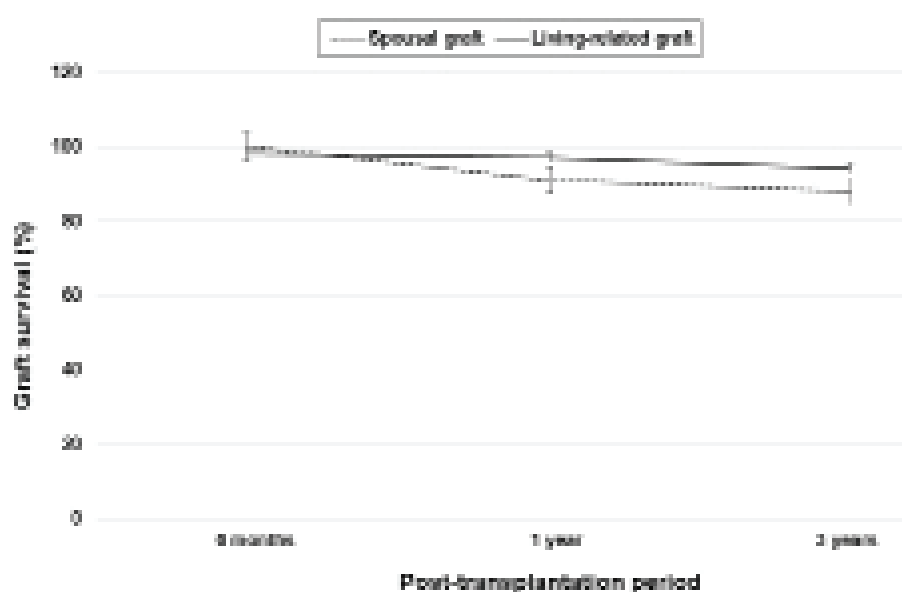


Fig. 1. Renal graft survival in spousal and living-related donor groups at 6 months, 1 year and 3 years post-transplantation.

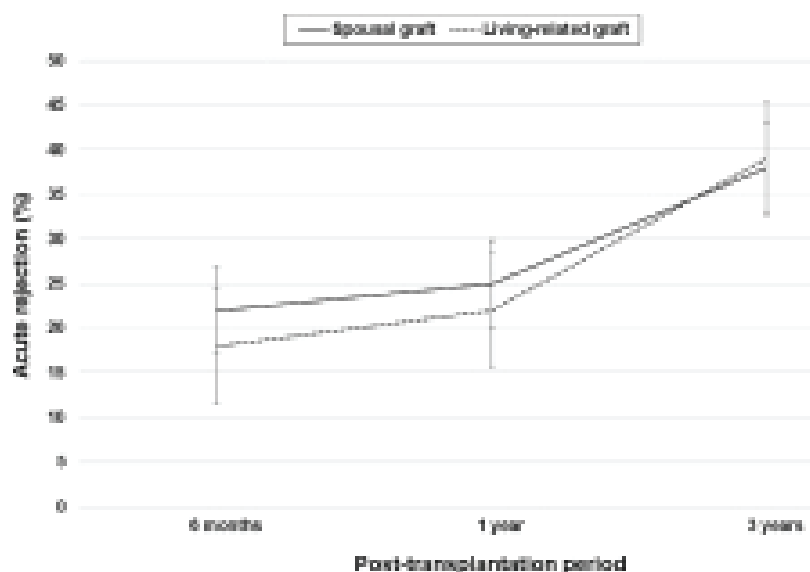


Fig. 2. Incidence of acute renal rejection in spousal and living-related donor groups at 6 months, 1 year and 3 years post-transplantation.

At 6 months, 1 year and 3 years post-transplantation, mean serum creatinine levels in graft recipients in the spousal donor group were 116.38 ± 17.72 $\mu\text{mol/L}$, 108.00 ± 13.61 $\mu\text{mol/L}$ and 112.88 ± 13.19 $\mu\text{mol/L}$, respectively; in the living-related donor group, the levels were 148.28 ± 8.03 $\mu\text{mol/L}$, 137.85 ± 6.16 $\mu\text{mol/L}$ and 139.39 ± 5.98 $\mu\text{mol/L}$, respectively ($P > 0.05$). At 3 years post-transplantation, no significant difference was observed in renal function in both groups.

Generally, spousal donors have a higher incidence of HLA mismatch than living-related donors (Table 3). For HLA-A, the number of spousal grafts with 2 HLA mismatches were significantly higher than living-related grafts (26% vs 3%, $P = 0.0004$). The number of spousal donor grafts with ≥ 1 HLA mismatch was significantly higher than living-related donor grafts for HLA-B (90% vs 70%, $P = 0.039$) and HLA-Cw (87% vs 58%, $P = 0.012$) loci. More patients (57%) in the spousal donor group had 2 HLA-B mismatches than patients (12%) in the living-related group ($P = 0.0002$). For HLA-Cw locus, 67% of patients in the spousal donor group had 1 antigen mismatch and 20% had 2 antigen mismatches; in the living-related donor group, 56% of patients had 1 HLA-Cw mismatch and only 2% had 2 antigen mismatches. The same finding was observed in HLA-DR and HLA-DQ loci. There was a higher incidence of 2 HLA-DR mismatches in the spousal donor group than the living-related donor group (44% vs 3%, $P = 0.004$). The incidence of mismatch that involved at least 1 HLA-DQB1 was also higher in the former than latter (80% vs 45%, $P = 0.033$).

There was a significant association between acute rejection risk and HLA mismatch regardless of donor type (Table 4). Although no antigen mismatch was observed in HLA-A, HLA-B and HLA-DR in 19 patients, none of them experienced graft rejection at 6 months post-transplantation. They also experienced the lowest rejection rates of 5% and 11% at 1 year and 3 years post-transplantation, respectively. Patients with ≥ 1 HLA mismatch have an increased risk of early graft rejection, and 24% of our patients experienced rejection episodes at 6 months post-transplantation ($P = 0.01$). Also, our study showed that the risk of rejection was 7 times higher at 1 year (29%, $P = 0.03$) and 3 years (46%, $P = 0.003$) post-transplantation.

Univariate analysis of each HLA locus showed the deleterious effects of antigen mismatch on HLA-A and HLA-B. Graft rejection rates in patients with HLA-A mismatch were 26% (OR, 2.69; $P = 0.04$), 31% (OR, 2.54; $P = 0.03$) and 51% (OR, 3.22; $P = 0.002$) at 6 months, 1 year and 3 years, respectively. In patients with HLA-B mismatch, the rejection rates were 25% (OR, 3.25; $P = 0.06$), 29% (OR, 2.56; $P = 0.07$) and 47% (OR, 2.68; $P = 0.02$) over the same period. The rejection risk was comparable between patients with and without mismatch for HLA-Cw at 6 months (21% vs 18%, $P = 0.64$) and 1 year (28% vs 20%, $P = 0.35$), but it was higher at 3 years in patients with HLA-Cw mismatch (48%) than those with a match (31%). However, the difference was not statistically significant (OR, 2.0; $P = 0.07$).

Table 3. HLA Mismatch in Spousal and Living-Related Renal Donors

HLA Type and Mismatch	Relationship Type		P Value
	Spouse (%)	Living-Related (%)	
HLA-A			
None	7 (23)	44 (41)	–
1	16 (51)	61 (56)	NS
2	8 (26)	3 (3)	0.0004
≥1	24 (77)	64 (59)	NS
HLA-B			
None	3 (10)	32 (30)	–
1	10 (33)	63 (58)	NS
2	17 (57)	13 (12)	0.0002
≥1	27 (90)	76 (70)	0.039
HLA-Cw			
None	3 (13)	41 (42)	–
1	16 (67)	54 (56)	0.035
2	5 (20)	2 (2)	0.001
≥1	21 (87)	56 (58)	0.012
HLA-DRB1			
None	3 (19)	15 (45)	–
1	6 (37)	17 (52)	NS
2	7 (44)	1 (3)	0.004
≥1	13 (81)	18 (55)	NS
HLA-AB			
None	1 (3)	17 (16)	–
1	3 (10)	37 (34)	NS
2	10 (33)	45 (42)	NS
≥3	16 (54)	9 (8)	0.002
≥ 1	29 (97)	91 (84)	NS
HLA-DQB1			
None	3 (20)	17 (55)	–
1	7 (47)	13 (42)	NS
2	5 (33)	1 (3)	0.008
≥1	12 (80)	14 (45)	0.033
HLA-ABDR			
None	1 (3)	17 (16)	–
1	3 (10)	30 (28)	NS
2	7 (23)	41 (38)	NS
≥3	19 (63)	20 (18)	NS
≥1	29 (97)	91 (84)	NS

HLA: Human leukocyte antigen; NS: Non-significant

Table 4. HLA Mismatch and Risk of Acute Renal Rejection at 6 Months, 1 Year and 3 Years Post-Transplantation

HLA Type and Mismatch	6 Months		1 Year		3 Years	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
HLA-A						
1	2.75 (1.02 – 7.40)	0.04	2.70 (1.11 – 6.59)	0.03	3.69 (1.71 – 7.97)	0.001
2	2.35 (0.50 – 11.02)	NS	1.69 (0.38 – 7.51)	NS	1.37 (0.36 – 5.19)	NS
>1	2.69 (1.02 – 7.11)	0.04	2.54 (1.06 – 6.09)	0.03	3.22 (1.52 – 6.81)	0.002
HLA-B						
1	2.98 (0.81 – 10.99)	NS	2.62 (0.90 – 7.63)	NS	3.0 (1.24 – 7.24)	0.01
2	3.91 (0.95 – 16.11)	NS	2.42 (0.72 – 8.21)	NS	2.06 (0.73 – 5.77)	NS
>1	3.25 (0.91 – 11.53)	NS	2.56 (0.91 – 7.20)	NS	2.68 (1.15 – 6.24)	0.02
HLA-Cw						
1	1.20 (0.46 – 3.10)	NS	1.41 (0.57 – 3.46)	NS	1.83 (0.84 – 3.99)	NS
2	1.85 (0.30 – 11.30)	NS	3.0 (0.56 – 15.87)	NS	5.54 (0.96 – 32.08)	0.04
>1	1.25 (0.49 – 3.17)	NS	1.52 (0.63 – 3.66)	NS	2.0 (0.93 – 4.32)	NS
HLA-DRB1						
1	2.67 (0.47 – 15.13)	NS	3.29 (0.59 – 18.27)	NS	1.30 (0.34 – 4.94)	NS
2	2.67 (0.30 – 23.43)	NS	4.80 (0.61 – 37.35)	NS	2.60 (0.46 – 14.63)	NS
>1	2.67 (0.50 – 14.22)	NS	6.67 (1.22 – 36.22)	0.01	1.56 (0.44 – 5.47)	NS
HLA-AB						
1	–	NS	4.76 (0.56 – 40.64)	NS	5.44 (1.11 – 26.78)	0.03
2	–	0.01	9.5 (1.18 – 76.73)	0.02	10.2 (2.15 – 48.46)	0.001
3	–	0.03	6.3 (0.71 – 56.29)	NS	5.84 (1.12 – 30.55)	0.04
4	–	0.03	9.0 (0.78 – 103.73)	NS	6.8 (0.95 – 48.69)	NS
≥1	–	0.01	7.28 (0.94 – 56.45)	0.03	7.30 (1.62 – 32.88)	0.003
HLA-DQB1						
1	5.94 (0.62 – 56.20)	NS	9.5 (1.05 – 82.26)	0.02	1.50 (0.39 – 5.84)	NS
2	12.67 (0.86 – 186.91)	0.03	19.0 (1.45 – 248)	0.01	6.00 (0.83 – 42.29)	NS
>1	17.1 (1.89 – 154.85)	NS	11.18 (1.29 – 96.65)	0.01	2.06 (0.58 – 7.35)	NS
HLA-ABDR						
1	–	NS	3.72 (0.41 – 33.52)	NS	5.02 (1.00 – 25.32)	0.0001
2	–	0.003	10.8 (1.33 – 87.91)	0.007	10.93 (2.27 – 52.65)	0.0007
3	–	0.04	6.6 (0.79 – 55.48)	NS	6.02 (1.23 – 29.57)	0.0008
4	–	NS	9.0 (0.78 – 103.73)	NS	10.63 (1.48 – 76.08)	0.02
5	–	0.01	18.0 (1.37 – 235.70)	0.03	8.5 (0.97 – 74.43)	NS
>1	–	0.01	7.38 (0.95 – 57.11)	0.03	7.27 (1.62 – 32.65)	0.003

CI: Confidence interval; HLA: Human leukocyte antigen; NS: Non-significant; OR: Odds ratio

With the recent introduction of HLA class II typing, data on HLA-DR and HLA-DQ were available in a third of our patients. HLA-DR mismatch was associated with increased rejection risk at 1 year (31%, $P = 0.01$), but

not at 6 months and 3 years. Patients with HLA-DQ mismatch were predisposed to early rejection risk at 6 months ($P = 0.05$) and 1 year ($P = 0.01$).

Discussion

Living-related kidney donors are more common than spousal kidney donors in Malaysia. To the best of our knowledge, this is the first study in Malaysia that reported on the potential of spousal donors as a safe option in renal transplantation despite a higher incidence of HLA mismatch than living-related donors.

In the literature, the benefits of spousal and other living-related donor transplantations have been reported in different populations.^{16,17} Terasaki et al¹⁸ reported that patient survival in spousal grafts were similar or even higher than grafts from parents with 1 HLA haplotype mismatch or other living donors. Our study found out that acute rejection episodes, graft function and patient survival at 6 months, 1 year and 3 years in recipients of spousal grafts were comparable to other living-related donor grafts. Additionally, Terasaki et al¹⁹ showed that—in the absence of pregnancy—the survival rate in wife-to-husband grafts was similar to husband-to-wife grafts. Due to the small number of spousal grafts and incomplete pregnancy data in our study, we could not replicate this finding.

Several reports have documented the viability of spousal transplantation in different Asian populations. For example, Tang et al²⁰ showed that despite a numerical difference between spousal and other living-related grafts in a Chinese population, the incidence of delayed graft function, acute rejection episodes, changes in serum creatinine level and graft or patient survival at 5 years did not reach statistical significance ($P > 0.05$). A recent Korean study on graft and patient survival in renal transplantation had shown comparable rates between spousal and living-related grafts.¹⁷ Kute et al⁵ also reported that recipients of living donor allograft from their spouses in India experienced an improvement in their marital, parent-child and sexual relations and family psychodynamics.

A comparative analysis of renal transplantation outcomes over a 20-year period had reported the influence of HLA mismatch on transplant function rate.²¹ This finding was corroborated by our study that showed a correlation between HLA mismatch and acute rejection risk regardless of donor types. However, our study also showed that not all classes of antigen mismatch are equally detrimental since HLA-Cw mismatch was not significantly associated with graft rejection up to 3 years post-transplantation. Instead, our study showed that HLA-A and HLA-B mismatch had a substantial negative effect on patient outcomes.

HLA class II antigens are reported to have lower levels of tissue expression compared to HLA class I antigens.²² However, findings on HLA-DR have shown that it plays an important role in renal transplantation. For example, Moore et al²³ have shown that increased HLA-DR mismatch

is associated with increased acute rejection risk and lowered graft survival. In acute rejection, expression of HLA-DR is induced on renal tubular epithelial cells by cytokines.²⁴ A multi-centre analysis of HLA matching has shown a steady fall in graft survival when the number of HLA mismatch increases—in combination with HLA-DR mismatch—to 6.²⁵ Additionally, logistic regression analysis in another study reported that HLA-DR mismatch is an independent predictor of subclinical inflammation after renal transplantation.²⁶ Our study found that HLA-DR mismatch poses a significant risk for the development of acute rejection at 1 year post-transplantation.

HLA disparity is not the only determinant of graft outcomes in spousal and other living-related renal transplantations. Factors such as graft quality,²⁷ HLA presensitisation,²⁸ cold ischaemic time,²⁹ age difference between donor and recipient³⁰ and compliance with immunosuppressant intake³¹ may also contribute to postoperative complications. In our centre, all transplantations are performed as scheduled procedures to prevent prolonged cold ischaemic time and immunosuppressants are initiated prior to surgery. Kuo et al³² reported that antibody induction was associated with a modest salutary effect on post-transplant acute rejection. Like most transplant centres, the immunosuppressive protocol in our centre comprise a calcineurin inhibitor (cyclosporine or tacrolimus), antimetabolite (mycophenolate mofetil) and steroid (prednisolone) that were administered during the maintenance period. Since most recipients of spousal renal grafts live with their donors, it may address the issue of non-compliance to immunosuppression medication-taking that is associated with negligence and postoperative depression.

Conclusion

Our study showed that HLA mismatch remains a valuable predictor of acute graft rejection in renal transplant patients in Malaysia. Although spousal donors have a higher incidence of HLA mismatch, overall no significant differences were observed in graft rejection risk, function and survival of living-related donor grafts. Consequently, spousal donors are a safe option and can address the shortage of kidney donors in Malaysia.

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