Transplant International

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Commercial transplants in local Pakistanis from vended kidneys: a socio-economic and outcome study

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Keywords

outcome, recipients, vended kidneys, transplants.

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Received: 26 October 2008 Revision requested: 16 November 2008 Accepted: 29 December 2008

doi:10.1111/j.1432-2277.2009.00836.x

Summary

Donor shortage and absence of transplant law lead to unrelated commercial transplants in Pakistan. We report the socio-economic and outcome parameters of 126 local recipients of unrelated kidney vendor transplants presenting to our institute between 1997 and 2007. Their outcome was compared with 180 recipients of living-related donor transplants matched for age, gender and transplant duration as controls. Age of commercial recipients was 35.63 ± 11.57 years with an M:F ratio of 2.4:1. Majority (92%) were transplanted in northern Pakistan paying US\$7271 ± 2198. All were educated with 50% being graduates or above and rich earning a monthly salary of US\$517 ± 518 with 44% earning >US\$500. Comparison of commercial recipients with controls showed high comorbidities 35 (28%) vs. 14 (8%) (P = 0.0001) with diabetes, hepatitis-C and cardiovascular diseases. Donor age was 29.97 \pm 6.16 vs. 32.63 \pm 9.3 years (P = 0.035). Biologic agents induction in 101 (80%) vs. 14 (8%) (P = 0.0001), acute rejections in 42 (33%) vs. 31 (17%) (P = 0.005), 1-year creatinine 1.84 ± 1.28 vs. 1.27 ± 0.4 mg/dl (P = 0.0001), surgical complications 28 (22%) vs. 14 (8%) (P = 0.001), tuberculosis 14 (11%) vs. 6 (6%) (P = 0.007), acute hepatitis 20 (16%) vs. 3 (2%) (P = 0.0001), cytomegalovirus 33 (26%) vs. 21 (11%) (P = 0.001) and recurrent urinary tract infection 35 (28%) vs. 30 (16%) (P = 0.034). Overall 1- and 5-year graft survival was 86% and 45% vs. 94% and 80%, respectively (P = 0.00001). Total deaths were 34 (27%) vs. 12 (6.0%) (P = 0.001). In conclusion, recipients of the vended kidneys are poor candidates, educated, rich and often self-selecting. Their outcome is poor, which will leave them poorer still and back to dialysis if not death.

Introduction

The incidence of end-stage renal disease (ESRD) in Pakistan is about 100 p.m.p. [1]. Paucity of dialysis and transplantation facilities in public and high costs in private sector renders more than 90% of our population disfranchised from renal replacement therapy [1]. The cost of dialysis in private sector is US\$20–25 per session and transplants cost between US\$6000–10 000 [1]. These are beyond the means of majority as per capita income is only US\$1000 per month [2]. Renal transplantation began

in the 1980s with living-related donors in the public sector [1]. However, with developing expertise in private clinics, lack of facilities in public sector, absence of transplant laws against commerce and shortage of organs have led to living unrelated donor transplants in the private sector from kidney vendors. The vendors are the poor and impoverished people of our society, majority of whom are in bonded labor living in villages of north eastern Pakistan. They sell their kidneys to earn freedom from bondage or pay off their loans [3]. Unlike the foreign tourists who return home and are cared for in

specialist centers [4-7], local vended kidney recipients often find themselves unable to obtain specialist care and proper follow-up, especially in case of complications requiring hospitalization. They present themselves at our Institute, a tertiary care center, which offers dialysis, living-related transplant and immunosuppressive drugs to all our patients free of cost [8]. Presently over 2000 recipients of living-related donor transplants are in follow-up at our institute. A number of reports have shown poor outcome and high infectious complications in tourist recipients who have purchased kidneys from Pakistan [4-7]. Many of these reports lack complete follow-up data, have small numbers, social and environmental difference, which makes it difficult to derive appropriate conclusions. Furthermore, there has not been any report on the outcome of our local Pakistani recipients of commercial transplants. In this study, we report the socio-economic status and transplant outcome of 126 of such recipients who presented at our institute between 1997 and 2007. Their outcome results were compared with that of local recipients of living-related donor transplants performed at our center. These controls were matched for age, gender and transplant date from our data base of over 2000 transplants for the same follow-up period.

Patients and methods

Our institution is the largest public sector organization in Pakistan offering dialysis, transplantation and immunosuppressive drugs free of cost to all patients. Although the institute is based in Karachi its catchments area encompasses the whole of Pakistan as all services are provided free as well as availability of specialist facilities of drug monitoring, immunologic screening, biopsy and imaging. Since 1986, over 2000 renal transplants have been performed from living-related family donors and as well as emotionally related spousal donors. All recipients as well as donors are followed-up in dedicated clinics with internationally accepted outcomes [1,8,9]. Recipients of living unrelated donor transplants from kidney vendors performed in private centers in the north of Pakistan present at our institute when they need specialist care not available in other private centers, or when they cannot afford the expense of post-transplant care vis-a-vis rejection, infections and drug monitoring. There are 195 outside transplant recipients in follow-up at our center. Of these, 69 were excluded as they received living, related donor transplants abroad in UK, USA, Bombay in neighboring India and other centers in Pakistan. We report the findings on the remaining 126 recipients of vended kidney who were transplanted from between 1993 and 2007 and who have come for follow-up at our institute from January 1997 to September 2007.

All information was recorded on a preset proforma. Informed consent was obtained from the patients or their family head. The proforma included information on demographics, socio-economic parameters, and pre/post-transplant medical history.

- 1 Demographics and socio-economic status: The proforma recorded age at transplant, date of transplant, date of enrollment at our center, city of residence, city and center of commercial transplant, education, profession, monthly household income, total expenses on transplant, sources of funds for transplant, cost of monthly immunosuppressive drugs and information on vendors to include gender, age and payment.
- 2 Medical history: Cause of renal failure, date of presentation at SIUT after transplant, graft function at 1 year with listing of medical comorbidities, post-transplant surgical and medical complications, post-transplant infections and causes of death.
- 3 Controls: The results of outcome, post-transplant medical and surgical complications, infections and causes of death in recipients were compared with recipients of living-related donor transplants from our data base of 2000 transplants. The controls were selected randomly who were matched for age at transplant, gender and date of transplant \pm 2 months. The period of transplants of the controls was the same as vended kidney recipients (1993–2007). In all 180 patients were found in the database to be eligible to fit our control criteria. Both recipients and donors were selected by standard criteria in this group of controls [10,11].

Immunosuppression was by triple drug regimen comprising cyclosporine, steroids and azathioprine or mycophenolate mofetil in the two groups. Induction by biologic agents was recorded wherever indicated.

Statistical analysis

Statistical analysis was performed by spss version 10.01 (SPSS Inc., Chicago, IL, USA). Data were presented as mean value \pm SD and percentage. Comparisons between the means were made by independent two-tailed t-test and chi-squared test was used to assess the association between two categorical variables. The level of significance was set at 0.05.

Results

The demographics and socio-economic parameters are detailed in Table 1. The mean age of the recipients was 35.63 ± 11.57 years with an M:F ratio of 2.4:1. Of the 126, 74 (59%) vendor-kidney recipients presented in

Table 1. Demographics and socio-economic parameters in recipients of vended kidney donor transplants (n = 126).

Parameter	Results	
Age at transplant years, mean (range)	35.63 ± 11.57 (15–61)	
Male:female ratio	89:37	
Presentation at our center		
Days after transplant,	771 ± 1220 (12–6094)	
mean (range)		
Out-patient	74 (59%)	
In-patient	52 (41%)	
No. donors in family,	1.99 ± 1.55 (0–6)	
mean (range)		
Reasons for vended kidney		
No. donors	26 (21%)	
Donor not willing	22 (17%)	
Blood group incompatible	43 (34%)	
Medical problem in donor	62 (49%)	
2nd and 3rd transplant	05 (4%)	
City/province of residence		
Karachi (Sindh)	84 (67%)	
Sindh	17 (13%)	
Punjab	15 (12%)	
Frontier Province	6 (5%)	
Balochistan	4 (3%)	
City of transplant		
Karachi (Sindh)	1 (0.8%)	
Rawalpindi (Punjab)	90 (71%)	
Lahore (Punjab)	26 (21%)	
Bombay (India)	9 (7%)	
Education		
Primary school	5 (4%)	
High school	16 (12.5%)	
College	44 (35%)	
Graduate	46 (36.5%)	
Postgraduate	15 (12%)	
Occupation		
White collar job	14 (11%)	
Self-employed	51 (40%)	
Skilled worker	31 (25%)	
Housewife	25 (20%)	
Student	03 (2.5%)	
Unemployed	02 (1.5%)	
Monthly household	517.54 ± 518.66	
income US\$, mean		
<100	12 (9.5%)	
100–500	58 (46%)	
501–1000	36 (28.5%)	
>1000	20 (16%)	
No. dependents in family, mean (range)	4.37 ± 2.32 (1–13)	
Cost of transplant US\$, mean (range)	7271 ± 2198 (2800–13500)	
Payment to vendor US\$ $(n = 55)$,	1801 ± 448 (830–4000)	
mean (range)		
Monthly cost immunosuppressive	200.1 ± 222.7 (17–1666)	
drugs US\$, mean (range)		

out-patient setting and the rest as in-patients with surgical, medical and infectious complications. Although the mean number of donors in the family was 1.99 ± 1.55 ,

21% of the vendor-kidney recipients reported that there were no donors in the family and 4% had retransplants where family donors were utilized. Majority had donors in the family who were willing; however, blood group incompatibilities or medical problems in 83% of the family members either singularly or in combination were the reasons for exclusion. Five of these recipients had undergone transplant workup at our center and were determined as unsuitable candidates for transplantation because of comorbidities, three with advanced diabetes and two being hepatitis C virus (HCV) RNA positive with chronic liver disease. More than three-quarters of the recipients were residents of Karachi, where our institute is situated and the rest were from other provinces: From Sindh 17, (100-600 km from Karachi), Puniab 15, (600-1200 km from Karachi), Balochistan 4 and Frontier Province 6, (900 km and 800-1600 km from Karachi, respectively). Majority of the transplants (71%) were carried out in Rawalpindi (1300 km from Karachi), Lahore (21%) (1000 km from Karachi) and (7%) were carried in Bombay, India. All recipients were literates and 51 (48.5%) were educated to graduate or postgraduate level. Of the recipients 65 (51%) were in business or were self-employed. About a third belonged to uppermiddle or rich class earning >US\$500 per month and only 9.5% were in lower-middle class earning <US\$100 per month. The rest were middle class working as skilled workers and in business. The mean cost of transplant was US\$7271 as a package including vendor payment and immunosuppressive drugs for a stay of 1 week. Of the 126, 59 (47%) vendor-kidney recipients financed the transplant from their own resources; for 37 (29%), the expenses were paid by their employers; 10 (8%) were funded by individual philanthropists and 20 (16%) by donations from Corporations. Information on vendor payment was given by 55 recipients where the vendors received a mean sum of US\$1801 ± 448 as payment for

Comparison of outcome of recipients of vended kidneys with that of recipients of living-related donor transplants is given in Table 2. In both the groups, the cause of ESRD was unknown mostly arising out of late presentation. Diabetes was more common and there was higher prevalence of hepatitis C in recipients of vended kidneys as compared with the controls. Biologic agents were used for induction in almost 80% of the recipients of vended kidneys; however, rejection episodes were much higher in this group of patients as compared with the controls. Although donors' data were available in only 55 cases, they were younger and predominantly males in the vended group as compared with controls. Serum creatinine at 1 year was significantly higher as compared with the living-related donor controls.

Table 2. Comparison of outcome in recipients of vended kidney donors with living-related donor transplants.

Parameters	Recipients of vended donors $(n = 126)$	Recipients of living-related donors (n = 180)
Original disease		
Chronic GN	16 (13%)	31 (17%)
Hypertension	32 (25%)	30 (17%)
Diabetic	15 (12%)	04 (2%)
Others	3 (2%)	18 (10%)
Unknown	60 (48%)	97 (54%)
Anti-HCV Positive	21 (16%)	19 (10.5%) (0.002)
Recipient age years	35.63 ± 11.57	33.68 ± 9.06 (0.22)
Male:female	89:37	131:49
Donor age years	29.77 ± 6.16 $(n = 55)$	32.63 ± 9.30 ($n = 0.035$)
Male:female	50:5	115:65
Induction	101 (80%)	14 (8%) (0.0001)
(biologic agents) %		
Acute rejection %	42 (33%)	31 (17%) (0.005)
Creatinine at 1 year mg/dl	1.84 ± 1.28	1.27 ± 0.44 (0.0001)
Creatinine < 1.5 mg/dl	67 (58.8%)	135 (80%) (0.003)
	n = 112	n = 169

Post-transplant complications are listed in Table 3. Frequency of surgical complications was found to be three times more in the vended kidney recipients. Multiple complications were observed in this group where four grafts had to be removed because of graft ruptures in two and abscesses in the other two. Other complications included penile amputation in two diabetic patients because of gangrene and blindness in one diabetic recipient. Three patients had post-transplant angioplasty and two had bypass surgeries. Similarly, medical comorbidities were significantly higher in vended kidney recipients. Diabetes and liver disease were more frequently encountered in this group. Four patients acquired post-transplant hepatitis B infection. Serious infections were significantly higher in the vended group as compared with the controls. Acute hepatitis led to liver failure and death in two and recurrent-urinary tract infection-caused graft loss in three recipients of vended kidneys.

The outcome measures of recipients of vended kidneys as compared with the controls are shown in Table 4. There were more deaths in the vended group and 13 recipients died with functioning grafts. Majority in the control group died with failed grafts. Of the 126 recipients of vended kidney, 51 (40.4%) are in follow-up in outpatient setting, where except for four all are buying their own medicines. Fifteen with failure are getting dialysis in other centers.

Of the 126, 105 were in regular follow-up at our center. The rest 21 had infrequent visits mainly because of

Table 3. Comparison of post-transplant complications in recipients of vended kidneys donors with living-related donor transplants.

	Recipients of vended kidneys	Recipients of living-related
Parameters	(n = 126)	donors ($n = 180$)
Surgical complication %	28 (22%)	14 (8%) (0.001)
Perigraft collection	3	5
Wound infection	6	2
Ureteric reimplantation	2	1
Urinary leak	5	1
Lymphocele	3	_
Re-anastomosis	1	1
Stricture urethra	1	1
Renal artery stenosis	3	1
Perigraft abscess	2	_
Graft PCN	2	_
Graft nephrectomy	4	_
Medical comorbid %	35 (28%)	14 (8%) (0.0001)
Diabetes	14	4
Cardiovascular disease	13	5
Chronic liver disease	9	4
Chronic lung disease	2	_
Hepatitis B	4	_
Recurrent disease	3	2
Infections		
Tuberculosis	14 (11%)	6 (6%) (0.007)
Acute hepatitis	20 (16%)	3 (2%) (0.0001)
Cytomegalovirus	33 (26%)	21 (11%) (0.001)
Recurrent urinary tract infection	35 (28%)	30 (16%) (0.034)

Table 4. Comparison final outcome of recipients of vended kidney donors with living-related donor transplants.

Parameters	Recipients of vended kidneys (n = 126)	Recipients of living-related donors $(n = 180)$
Total death	34 (27%)	12 (6.0%) (0.001)
Sepsis	14	6
Cardiovascular	10	5
Liver failure	08	0
Others	02	01
Death with function	13 (10%)	2 (1.0%) (0.001)
Dialysis	23 (18.2%)	9 (5.0%) (0.0001)
At center	08	09
Outside center	15	_
Follow-up at center	51 (48.5%)	159 (88.0%)
Other center	10 (9.0%)	_
Lost to follow-up	8 (6.3%)	_

residence in other cities or abroad. Of these six have died, seven are on dialysis in other cities and eight have been lost to follow-up as they were non responders to our follow-up calls. The characteristics of these patients are given in Table 5.

Table 5. Characteristics of patients lost to follow-up.

Patient no.	City of residence	Last S. Cr (mg/dl)	Days after transplant	Reason for presentation
1	Lahore	1.26	785	Malaria
2	Rawalpindi	2.30	1457	Cyclosporine level
3	Rawalpindi	2.56	285	Dysfunction and biopsy
4	Lahore	1.86	1435	Cyclosporine level
5	Quetta	2.78	1235	Hepatitis B infection
6	Rawalpindi	2.14	1487	Tuberculosis
7	Peshawar	3.15	743	Graft dysfunction
				and biopsy
8	Rawalpindi	2.34	1858	Cyclosporine level

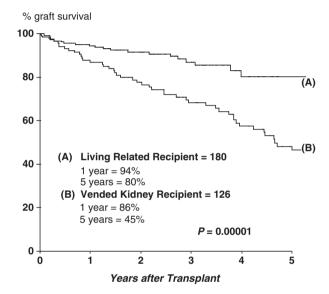


Figure 1 Comparison of graft survival between recipients of vended kidney donor versus recipients of living-related donor transplants.

Death-censored graft survival of recipients of vended kidney recipients and controls is given in Fig. 1. The eight recipients who were lost to follow-up were censored at their last follow-up date. One- and 5-year graft survival was poorer in recipients of vended kidneys as compared with controls 86% vs. 94% at 1 year and 45% vs. 80% at 5 years (P = 0.00001), respectively.

Discussion

Renal transplantation is the ultimate therapy for endstage renal failure as it offers a better quality of life and longer survival as compared with dialysis [12,13]. Worldwide organ shortage and death on waiting lists have resulted in renal failure patients seeking transplants in developing countries, where organs can be procured [14]. A number of reports have appeared in the literature

showing poor outcome and infectious complications in recipients of vended kidneys from Pakistan [4-7]. However, there has not been a study on local recipients of vended kidneys. This study reports socio-economic aspects and outcome of local recipients of vended kidneys who presented at our center for follow-up care. Renal transplantation in Pakistan started from living-related altruistic donors [1]. However, shortage of organs resulting from absence of deceased donors and lack of facilities in the public sector have led to transplants from unrelated paid donors in the private sector. Maximal activity from commercial transplants was 2000 per year in 2007 [3] where approximately 1500 (75%) were for transplant tourists and 500 for locals. Unfortunately, this could not fulfill the needs as the incidence of ESRD is 100 p.m.p i.e. 16 000 cases per year calculated from a population of 160 million [2].

Socio-economic analysis has shown that the recipients of vendor kidneys were educated and well-to-do individuals of our society with established jobs or businesses. Almost one-third of them financed the transplants from their own resources while the rest had access to funds through employers and corporations. There are interesting socio-economic similarities between our transplant recipients and the transplant tourists who came to Pakistan from USA, UK and Canada [5,7,15]. These studies have shown that transplant tourists were predominantly of Asian origin, males, educated and financially strong and in some countries of their domicile, they were reported to be financially better off than the local population waiting for transplant [15,16]. Many tourists traveled to their country of origin in Pakistan [5,7,15,16]. To sum up, the ones who seek commercial transplants are educated, better-placed, financially sound foreigners, predominantly of Asian origin, who may not have willing donors because of cultural reasons or who may want to avoid use of willing donors and who are also unlikely to get deceased donors because of blood group and human leukocyte antigen (HLA) disparities within races. They, therefore, seek transplants elsewhere rather than die on the waiting list or wait for a donor to come along as in our local cases. These are the people who are perhaps the main reason behind the development of transplant tourism in our region [17].

In unrelated commercial transplants, there is absence of knowledge of HLA matching. The use of biologic agents in 80% of the recipients suggests that their use was perhaps a tool to counter HLA disparity as reported by one of the local commercial centers [18]. The use of biologic agents may prevent early rejections; however, higher rejection episodes than controls suggests that there was inadequate screening for pretransplant antibodies as well as monitoring of immunosuppressive drugs. Majority of

the donors used were young male subjects to confer the benefit of better graft function and survival as donor age has been reported to be one of the important factors for graft outcome [19]. Furthermore, there may well be a price tag for young donors as some paid up to US\$13000 for a kidney.

The mean creatinine at 1-year was higher in the recipients of vended kidneys and graft function of creatinine <1.5 mg/dl was significantly low in this group as compared with controls. This may be attributed to the impact of higher rejections episodes [8] and poor drug monitoring and follow-up in the early transplant period. A number of studies have shown graft survival in commercial transplants of around 90% at 1 year while others have shown below 50% [20]. Graft outcome in our local commercial recipients was far inferior to our living-related transplants. This experience is similar to that reported from Canada and Turkey where similar comparisons were made with living-related donors transplants [7,21].

A number of studies have reported high post-transplant surgical and medical complications [5,6,20,21]. Our experience is similar as surgical complications were thrice of those found in controls. Some of the complications encountered are of early transplant period, which should have been dealt with at the transplant center. Perhaps the 1- to 2-week package results in early discharge in disregard of consequences. These also suggest that the surgical skills and aseptic conditions may well be below standard. Therefore, a number of recipients presented with infectious wounds, open wounds and ureteric leaks requiring procedures at our center to salvage the grafts. Unfortunately, in some cases severe infections necessitated graft nephrectomy to be the only option.

One of the reasons for poor outcome in these recipients is the presence of comorbidities before transplantation. Diabetes, cardiovascular disease and chronic liver disease would have excluded many of these recipients from transplantation if proper evaluation was undertaken. Similar to our experience, high rates of infections have been reported in several studies where hepatitis B, C and tuberculosis (TB) were observed frequently in recipients of commercial transplants [20]. It can be suggested that there was HCV RNA positivity in these recipients pre transplant, which was perhaps not tested. Furthermore, the reported high prevalence of hepatitis B and C in vendors [22] may also contribute to acute hepatitis in these recipients. There may well be also the effect of overimmunosuppression by the use biologic agents as seen by high rates of cytomegalovirus, TB and perhaps aggravation of hepatitis C leading to liver failure as seen in eight of our cases. Another reason for poor outcome in these

recipients may have been transplantation against the physician advice and perhaps self-selection. As reported earlier in other studies many patients undergo transplant against the advice of their physicians [4,6,7,23]. In fact, five of the recipients were determined to be unsuitable candidates for transplant at our center because of complicated diabetes and liver disease. These observations suggest that the interest of physician and surgeons of commercial centers appear to be only commerce-driven without regard of the suitability of the recipient for transplant or, for that matter, the outcome of vendor. This is confirmed by the study showing poor heath status and high prevalence of hepatitis B and C in vendors from Pakistan [22]. Therefore, inadequate recipient evaluation and poor selection may significantly contribute to the inferior outcomes both in terms of graft and patient sur-

In the final analysis, commercial transplants in Pakistan failed to fulfill the local needs with poor patient and graft survival. In our experience, a quarter of the recipient died, unfortunately a third of them with functioning grafts. More than half of the grafts have been lost majority within 5 years of transplantation. Self-selection and poor pretransplant evaluation in private centers contribute to this outcome. The driving force in commercial centers was financial gains with little regard for the outcome of the recipients or vendors. Fortunately, with the promulgation of transplantation law in Pakistan, commercial transplant are now in negligible numbers carried out in clandestine centers.

Presently about half of the recipients are in follow-up at our center and a quarter on dialysis. Many have failing grafts which require extreme care and newer Immunosuppression to salvage the grafts as long as possible. We may be able to do this in some but for others with complicated diabetes, cardiovascular and liver disease the outlook is poor. The limitation of our study is that this is a small number as compared with hundreds of other who have received commercial transplants in Pakistan. The manner in which they have failed can only be speculated. Judging from the published reports and our own experience suggests that commercial transplants have a poor outcome both in terms of grafts and patients survival.

In conclusion, recipients of the vended kidneys were rich, educated individuals who also might have been poor transplant candidates who often resorted to self-selection. They wanted to live – not knowing that their outcome will be poor leaving them poorer still and back to dialysis if not death. Physicians and patients both need to be warned about the risk and poor outcome of commercial transplant in Pakistan or any other new center in any part of the world.

Authorship

SAHR: study design, development of questionnaire, drafting of manuscript, critical review and final approval. SAAN: study design, development of questionnaire, data acquisition and analysis, drafting of manuscript and revision and final approval. MNZ, RN, EA and FA: study design, development of questionnaire, data acquisition and analysis, drafting of manuscript and critical review. FM and RM: study design, data acquisition and analysis, drafting of manuscript and critical review.

Funding

SIUT Research Fund.

Acknowledgements

We are grateful to Ms Sakina Yousuf for statistical analysis and Mr Hobin Daniel for preparation of manuscript.

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