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Outcome of ABO-Incompatible Living Donor Kidney Transplantation: A Single Center Observational Study from Nepal

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ABSTRACT

Introduction

Kidney transplantation is the most effective treatment for end-stage renal disease (ESRD) patients. However, the increasing number of ESRD patients and the limited availability of living and cadaveric donors has led to a growing waiting list for kidney transplantation. ABO-incompatible transplantation has emerged as an alternative for these patients in Nepal.

Methods

This was an observational study of all the patients who underwent kidney transplantation from March 2017-Feb 2019. Data on demography of recipients and donor, blood group, human leukocyte antigen mismatch, induction agent, post-operative complications and creatinine clearance at discharge and one-year post-transplant were collected and analysed. Then we compared patient and kidney graft survival at one year between ABO incompatible and ABO compatible recipients.

Results

During the study period, there were total of 124 kidney transplant recipients among them 12 were ABO incompatible and 112 were ABO compatible recipients. The study showed slightly lower patient and graft survival in ABO-incompatible recipients than ABO compatible recipients (83.3% vs 99.2%, p<0.001). However, death-censored graft survival were similar in both groups (100%,p<0.001). The graft function at one year measured by creatinine clearance was better in ABO-incompatible recipients than ABO-compatible recipients (67.1±11.75 vs 61.87±12.82, p<0.001). Postoperative complications were slightly higher, however, complications at one year were lower in ABO-incompatible recipients.

Conclusion

The study showed that living donor ABO-incompatible kidney transplant recipients have a good outcome at one year but is associated with greater risks of patient and graft loss at early transplant period compared to ABO-compatible recipients.

Keywords
ABO incompatible; graft survival; infection; kidney transplantation; patient survival; rejection

INTRODUCTION

Kidney transplantation is the most effective treatment available for end-stage renal disease (ESRD).[1] Due to a growing number of ESRD patients, the waiting list of kidney transplantation is increasing. There is a strict living-related kidney donor program and limited availability of cadaveric donor program, hence ABO incompatible transplantation has emerged as an alternative to these patients in Nepal.[2]

ABO-incompatibility was once considered a contraindication to kidney transplantation.[3] Until a breakthrough study formulated a desensitization protocol.[4] This led to wider utilization of the procedure in Japan in the late 1980s, USA in the mid 1990s, and Europe in the early 2000s.[4-6]

ABO incompatible kidney transplantation was started in Nepal in 2017.[2] Few data are available about the long term survival of the recipients with ABO incompatible transplantation.[7-9] The study aimed to evaluate the outcome of ABO incompatible transplantation at one year in terms of patient and graft survival. The subgroup analysis include peri-operative complications and complications at one year, induction agent, mode of dialysis, native kidney disease and human leukocyte antigen (HLA) mismatch.

METHODS

It was a retrospective observational study which analysed all the living donor kidney transplantation at Department of Nephrology and Transplantation Medicine Tribhuvan University Teaching Hospital from March 2017 to Feb 2019. Prior approval was taken from the Institutional Review Committee (IRC) of Institute of Medicine. Data recorded included donor and recipient age and gender, blood group, HLA mismatch, induction agent, post-operative complications and creatinine clearance at discharge and one year post transplant. Patients survival, refers to time from kidney transplant to patients death. Graft survival refers to time from transplant to kidney graft failure. Graft failure refers to need to resume the dialysis in the kidney transplant recipient, and was calculated as creatinine clearance measured by Cockcroft-Gault equation.

The data was recorded as per the working proforma, continuous data was presented as mean with standard deviation (SD) and compared using paired t-test, and the categorical data were compared using Chi-square test. Patient and graft survival was calculated by Kaplan-meier curve and compared between the groups by log-rank test. A p-value <0.05 was considered statistically significant. Analysis was performed using SPSS software ver 20.

RESULTS

A total of 124 patients were included in the study among them 12 were ABO incompatible (ABOi) recipient and 112 were ABO compatible (ABOc) recipients.

The ABOi donors had a mean age of 46.75±8.55SD, and nine of the 12 donors being female. Similarly the ABOi recipients had mean age of 32.5±12.2 SD and eight of them being males. ABOc donors had mean age of 46.9±10.84SD, 77 of them being females. Similarly in the ABOc recipients had mean age of 34.6±9.8 SD, 93 of them being males.

Among 12 ABOi recipients Antithymocyte globulin(ATG) was used as induction agent in seven patients, nine had HLA mismatch of less than three, and nine had blood group of A positive. Similarly in 112 ABOc recipients ATG was used in 108 patients, 80 patients had HLA mismatch of less than three as shown in Table 1.

Among 12 ABOi recipients, 10 patients were alive during the first year and the two patients died.

Table 1. Baseline profile of the recipients and donor

Parameters	ABO incompatible		ABO compatible	
	Recipients	Donor	Recipients	Donor
Age (Mean±SD)	32.5±12.2	46.75±8.55	34.6±9.86	46.9±10.84
Sex	8			
Male	(66.6%)	3 (25%)	93 (83.03%)	35 (31.25%)
Female	4 (33.3%)	9 (75%)	19 (16.9%)	77 (68.75%)
HLA mismatch				
0-3	9 (75%)		80 (71.42%)	
4-6	3 (25%)		32 (28.58%)	
Induction agent				
ATG	7 (58.33%)		108 (96.4%)	
Basiliximab	5 (41.6%)		4 (3.56%)	

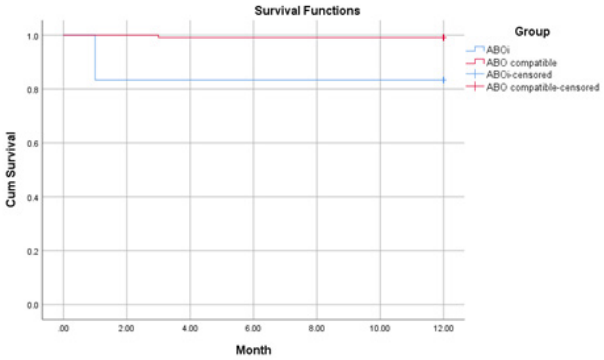

Figure 1. Patients survival at one year

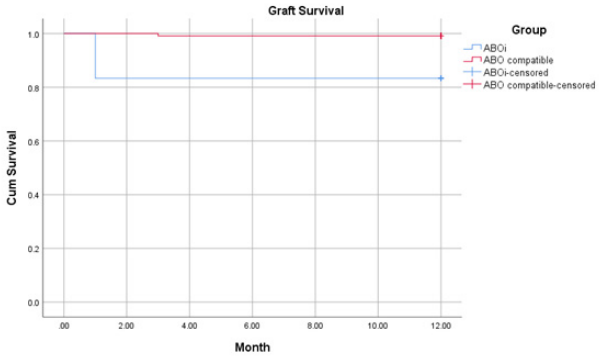

Figure 2. Graft survival, death censored graft survival at one year

Among the patients who did not survived during the first year the cause of death was ABMR followed by sepsis in one patient and shock in the other, and both of them died with the functioning graft in the first month of transplantation. Among 112 ABOc recipients 111 patients survived at one year, one patient died due to surgical complication. The patients survival at one year in ABOi and ABOc recipients was 83.3% and 99.2%.(P<0.001) as shown in Figure 1.

In the ABOi, graft survival and death censored graft survival was 83.3% and 100%, and in ABOc recipients the graft survival and death censored graft survival was 99.2% and 100%. Overall graft survival was low in ABOi recipient however death censored graft survival was similar in both the groups(p<0.001) as shown in Figure 2.

The creatinine clearance of ABOi recipients at discharge was 62.1±11.75 and 67.1±14.16 at one year. Similarly in the ABOc recipients the creatinine clearance at discharge was 58.47±15.34 and at one year it was 61.87±12.82. The graft function was better in ABOi recipients at one year(p<0.001) as shown in Table 2.

In the ABOi recipients medical complication was seen in six patients with UTI being the common complication seen in four patients, antibody mediated rejection (ABMR) seen in one patients and three patients had surgical complications. Similarly in ABOc recipients medical complications were seen in 22 patients with UTI seen in 10 patients, acute cellular rejection(ACR) in one, antibody mediated rejection in one patient. Similarly nine patients had surgical complications as shown in Table 3.

Among the ABOi recipients, 3(30%) patients were hospitalized for pneumonia and cryptococcal

Table 2. Creatinine clearance at discharge and one year

Creatinine clearance	ABOi recipients (n=12)	ABOc recipients (n=112)	p value
Discharge	62.1±11.75	58.47±15.34	<0.001
One year	67.1±14.16	61.87±12.82	<0.001

Table 3. Post-operative complications

Complications	Number (%)	
	ABOi recipients (n=12)	ABOc recipients (n=112)
UTI	4 (33.3%)	10 (8.9%)
Pneumonia	1 (8.3%)	4 (3.57%)
Delay Graft Function	0	6 (5.3%)
ACR	0	1 (0.89%)
ABMR	1 (8.3%)	1 (0.89%)
Hematoma	0	4 (3.57%)
Dissection	1 (8.3%)	0
Re-anastomosis	1 (8.3%)	2 (1.78%)
Renal artery stenosis	1 (8.3%)	3 (2.67%)

Table 4. Complications at one year

Complications	Number (%)	
	ABOi recipients (n=12)	ABOc recipients (n=112)
Pneumonia	2 (16.66%)	4 (3.57%)
PTDM	0	9 (8.03%)
ABMR	0	4 (3.57%)
ACR	0	8 (7.14%)
FSGS recurrence	0	4 (3.57%)
Sepsis	0	2 (1.78%)
BK virus nephropathy	0	2 (1.78%)
Cryptococcal meningitis	1 (8.33%)	0
Pulmonary TB	0	2 (1.78%)

meningitis, similarly 35 (31.25%) ABOc recipients had complications, among them Post transplant diabetes mellitus (PTDM) was seen in nine patients, ACR was seen in eight patients, ABMR, FSGS recurrence and pneumonia were seen in four patients. Sepsis, BK virus nephropathy and pulmonary tuberculosis were seen in two patients as shown in Table 4.

The most common cause of CKD among ABOi recipient as well as in ABOc recipients was chronic glomerulonephritis(CGN). There were seven pre-emptive transplantation in ABOc recipients and two patients in ABOc recipient were on peritoneal dialysis as shown in Table 5.

DISCUSSION

With the increasing number of patients with ESRD, obtaining a living-related compatible kidney transplantation has become more challenging, leading to ABO incompatible kidney transplant as a safe and alternative way to shorten the waiting time for a renal graft.

In this study a total of 12 ABO incompatible kidney transplant recipient along with 112 ABO compatible kidney transplant recipient were included. The initial studies had shown a graft survival of 79% and patient survival rate of 88% at 1 year,[7] subsequent studies have shown improved patients and graft survival, due to improved immunosuppression protocols.

Study done in Japan found comparable patient and graft survival rates between ABOi and ABOc recipients, with most rejections occurring in ABOi recipients within the first month after transplantation, suggesting that successful graft function in ABOi recipient requires keeping antibody level at safe level in the initial post-operative period.[11]

A meta-analysis found 96% and 98% patient survival rate of ABOi and ABOc recipients at one year post transplant, with infection being the most common cause of death.[9,12] Complications like infection, antibody mediated rejections were more common in ABO incompatible recipients during the period.[12]

Studies have shown a graft survival of over 94% and patient survival of more than 95% in ABO incompatible recipients.[10-12] However domestic reports on ABO incompatible kidney transplantation are few. Our study of 12 ABO incompatible recipients performed since March 2017 showed a patient and graft survival rate of 83.3% at one year, and death censored graft survival was 100% in both the ABOi and ABOc recipients. Two ABO incompatible patients who died, one of them developed ABMR and died due to sepsis and the other died due to shock with the functioning graft. Post-operative complications were higher in ABO incompatible recipients, however complications at one year was lower than ABO compatible recipients.

CONCLUSION

The result from our studies shows that living donor ABO incompatible kidney transplant recipients have good outcome at one year but is associated with greater risk of patient and graft loss at early transplant period compared to ABO compatible recipients.

Table 5. Native kidney disease and mode of dialysis in patients

Native kidney disease	ABOi recipients (n=12)			ABOc recipients (n=112)			
	HD	PD	Total	HD	PD	Preemptive	Total
CGN	9 (75%)	0	9	70 (62.5%)	1 (0.9%)	5 (4.5%)	76
IgAN	0	0	0	6 (5.4%)	0	0	6
Diabetes	1 (8.3%)	0	1	8 (7.1%)	1 (0.9%)	2 (1.8%)	11
SLE	0	0	0	3 (2.7%)	0	0	3
MPGN	0	0	0	3 (2.7%)	0	0	3
ADPKD	0	0	0	3 (2.7%)	0	0	3
Obstructive Uropathy	1 (8.3%)	0	1	3 (2.7%)	0	0	3
VUR	0	0	0	3 (2.7%)	0	0	3
FSGS	0	0	0	2 (1.8%)	0	0	2
Alport syn-drome	0	0	0	2 (1.8%)	0	0	2
Crescentic glomerulonephritis	1 (8.3%)	0	1	0	0	0	0
Total	12	0	12	103	2	7	112

Note:cgn-chronic glomerulonephritis, IgAN- IgA nephropathy, SLE-systemic lupus erythematosus, mpgn-membranoproliferative glomerulonephritis, ADPKD-autosomal dominant polycystic kidney disease,vur-vesicoureteral reflux, fsgs-focal segmental glomerulosclerosis.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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