



## COMPLICATIONS AFTER KIDNEY TRANSPLANTATION: A PROFILE OF 103 PATIENTS FROM A TERTIARY CARE CENTER

### Nephrology

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### ABSTRACT

**Background:** End Stage Renal Disease (ESRD) requires renal replacement therapy (RRT) such as Haemodialysis (HD) or Peritoneal Dialysis (PD) or Kidney Transplantation (KT). The purpose of RRT is to prolong life and maintain quality of life. The history of renal transplantation illustrates the successful integration of the fields of surgery, medicine and immunology, reflecting the development of healthcare in modern era which has improved the quality of life of the transplant patients. Low survival rates and a relatively poor quality of life on HD make KT an attractive treatment alternative with good clinical results even in elderly patients with comorbidities.

**Objectives:** This was an observational study conducted in an established kidney transplant unit at a single tertiary care center in India. The objectives of our study were to analyse surgical complications in renal transplant recipients following deceased donor and live donor (ABO compatible or incompatible) kidney transplants and compare it with contemporary literature and to identify possible risk factors related to KT recipient characteristics associated with surgical complications.

**Methods:** We studied the case records of patients who underwent KT at our center from January 2015 – December 2015.

**Results:** The total number of surgical complications observed was 44 out of 103 KT surgeries in 35 patients (33.9%). Nine (8.7%) patients had multiple complications while 26 (25.2%) patients developed a single surgical complication. Urological complications were seen in 25 (24.3%) patients and they constituted 59% of all surgical complications. Urinary Tract Infection (UTI) was seen in 24 patients (23.3%). No patient developed a ureteric leak. Diabetes was found to be more common amongst patients with UTI and wound infections.

**Conclusion:** The complication rates observed at our center were in line with expected rates based on available literature. KT remains a complex procedure, which should be performed at centers with high-volume experience. We hope that this study adds to the body of literature on the subject of KT.

### KEYWORDS

ABO compatible, ABO incompatible, Deceased donor kidney, Surgical complications, Renal Transplant, Urinary Tract Infections

### 1. INTRODUCTION

End Stage Renal Disease (ESRD) requires renal replacement therapy (RRT) such as Haemodialysis (HD) and Peritoneal Dialysis (PD) or Kidney Transplantation (KT) for the patient to survive. The purpose of KT is to prolong and maintain the quality of life. The history of renal transplantation illustrates the successful integration of the fields of surgery, medicine and immunology, reflecting the development of healthcare in modern era which has improved the quality of life of the transplant patients<sup>1</sup>. KT is considered the most cost-effective therapy for ESRD<sup>2</sup>. Low survival rates and a relatively poor quality of life on HD make kidney transplantation an attractive treatment alternative with good clinical results even in elderly patients with comorbidities<sup>3</sup>. Despite improvements in surgical techniques, surgical complications (SC's) following kidney transplantation remain an important clinical problem that increase morbidity, hospitalisation and costs, and sometimes cause mortality<sup>2,4</sup>. Several risk factors for SC's among kidney transplant candidates have been observed, and SC's do not necessarily imply a surgical procedure-related technical problem<sup>4</sup>.

Retrospective studies have reported the incidence and risk factors for SC's in renal transplant patients; however, reports from Indian centers are few. In addition, considering the recent reports of increased SC's with use of newer immunosuppressant agents, not all studies have included the newer immunosuppressant mTOR inhibitors in their analysis. Therefore, it is desirable to analyse these risk factors with the ultimate goal of reducing the incidence of SCs.

The magnitude of end-stage renal disease (ESRD) in India still remains largely undetermined. It is estimated that around 220,000 patients require KT in India and close to 7500 KT's are done annually, of which 90% are from living donors, and 10% from deceased donors<sup>5</sup>.

### 2. OBJECTIVES

This was an observational study to analyse surgical complications in kidney transplant recipients following deceased donor and live donor (ABO compatible or incompatible) kidney transplants and compare it with contemporary literature. We also wanted to identify risk factors related to recipient characteristics associated with surgical complications.

### 3. MATERIALS AND METHODS

#### 3.1 Study location and design

The study was conducted at a single tertiary care centre. All patients who underwent renal transplant from January 2015 to December 2015 were included in the study. Patients of all age groups and either sex were included in the study. Patients received either live (related or unrelated) ABO blood group compatible or ABO blood group incompatible kidney or deceased donor kidney. All transplants were performed by one of five senior surgeons highly trained and experienced in KT using standard surgical techniques.

Routine post-operative anti-coagulation therapy was not used, unless medically indicated. After surgery, the patients were monitored clinically and biochemically.

In addition, patients underwent a transplant kidney Colour Doppler flow study, Isotope renal scanning (DTPA) and transplant kidney biopsy, when indicated.

All enrolled patients underwent KT as per standard practice and all perioperative parameters were collected. They were also followed at 6 months in the Department of Urology with post-transplant USG / Colour Doppler of transplanted kidney and serum creatinine reports.

#### 3.2 OPERATIVE TECHNIQUE

Patients underwent KT as per the standard protocol after ensuring sterile urine. Antibiotic prophylaxis was given to all the patients. Silastic Foley catheterisation was done in sterile field and kept accessible to the operating team. Right iliac fossa / modified Gibson's was the skin incision of choice, irrespective of the side of donor nephrectomy. Left iliac fossa incision was used in previously operated KT cases. External oblique aponeurosis, internal oblique muscle and transverses abdominus muscles were incised in line of skin incision to reach retroperitoneal cavity and allow exposure of common iliac vessels cranially and up to femoral canal distally. Lymphadenectomy was done over external iliac vessels to prepare the vein for KT. Internal iliac artery was ligated and cut just proximal to its anterior/posterior division and was the most common artery used for anastomosis. Only in cases of severely atherosclerotic artery or poor flow or narrow caliber in internal iliac artery, was the external iliac artery used. Renal

vein was usually anastomosed to external iliac vein and neoureterocystostomy done in Lich - Gregoir fashion. DJ stent was not kept routinely and used only in cases of fragile bladder mucosa, narrow ureteric orifice and on all deceased donor transplants in view of questionable vascular integrity of the donor ureter. Tube drain was routinely kept behind the kidney and removed on 7<sup>th</sup> post-op day when drainage was <25ml in 24 hours. All complications were noted and managed as per standard protocols.

### 3.3 IMMUNOSUPPRESSION

Standard immunosuppressive treatment used was triple drug regimen consisting of mycophenolatemofetil (MMF), tacrolimus (CNI) and steroids. Sirolimus was not used de novo; however, tacrolimus was replaced with sirolimus in patients who developed CNI toxicity. MMF was given at a standard dose of 500 mg PO three times daily. Tacrolimus was given at a dose of 0.12 mg/kg in two divided doses. Doses of Tacrolimus were titrated to trough levels of 8-12 ng/mL in the early transplant period, then to 5–10 ng/mL 3 months later. Across the blood group recipients received Rituximab 7 days prior to and on the day of transplant and 4 days post-op period in the doses of 375 mg/m<sup>2</sup>. Plasmapheresis was done 7 days before surgery and on the 2<sup>nd</sup> day in post-operative period as a part of the protocol.

### 3.4 OUTCOME EVALUATION

Complete blood counts, blood urea, serum creatinine and serum electrolytes were performed postoperatively in all cases. Fever of >100° F was considered significant. On postoperative day 3, USG Colour Doppler of the transplant kidney, ureter and bladder was obtained. Serum creatinine was done every alternate day. Foley's was removed on 5<sup>th</sup> and drain removed on 7<sup>th</sup> day. Isotope renal scan (DTPA) was done on 10<sup>th</sup> post-op day or a day before planned discharge. DJ stent, if inserted, was removed at 3 weeks or earlier if urine culture showed >20,000 CFU in males and >50,000 CFU in females but before the discharge of the patient. Blood transfusion was considered for patients with significant blood loss, significant decrease in haemoglobin levels or patients with signs of hypovolemia, refractory to crystalloid or colloid reposition.

### 3.5 DATA COLLECTION

Demographic and clinical data were collected at the time of KT and during hospitalization until discharge, by case file review, in the medical records department (MRD) and in the kidney transplant register of the hospital. Finally, all recipients with a documented SC during the first 6 months after surgery were identified. This included analysis of patients with prolonged stays after kidney transplantation and re-admissions.

### 3.6 STATISTICAL METHODS AND ANALYSIS

Quantitative data was represented as descriptive statistics such as proportions, means or medians. P value <.05 was considered statistically significant. Qualitative data was represented as complications in term of blood loss, duration of operation, duration of stay in hospital etc.

Association between qualitative variables was assessed by Chi-Square test with Continuity Correction for all 2 X 2 tables and with or without Continuity Correction in rest and Fisher's Exact test for all 2 X 2 tables where p-value of Chi-Square test is not valid due to small counts. In presence of small counts in tables in more than two rows and/or columns, adjacent row &/or Column data was pooled & Chi-Square Test reapplied with Continuity Correction for all 2 X 2 tables and with or without Continuity Correction in rest and Fisher's Exact test for all 2 X 2 tables where p-value of Chi-Square test is not valid due to small counts in spite of pooling of data.

To assess the predictor variables of achieving success of transplant, Binary Logistic Regression was applied between 'Success as Outcome' as dependent variable & Surgical Complication as independent (Predictor) variable.

Results were graphically represented where deemed necessary. Appropriate statistical software, including but not restricted to Microsoft Excel, SPSS version 25 (IBM, NY, USA) was used for statistical analysis. Graphical representation was done in MS Excel 2010.

### 3.7 Scientific committee & ethical committee approval

This study was approved by the Institutional Ethics Committee and

Scientific Committee of the Hospital.

## RESULTS

A total of 103 patients met the inclusion criteria of the study. Demographic data is shown in Table 1. Most recipients were male (76, 73%), and most of the donors were ABO compatible donors (74, 72%). Most were diabetic (83, 80%). Average duration of stay was 22 days. There were a total of 44 surgical complications in 35 patients, with a slight female preponderance which was not statistically significant. (Tables 2,3)(Figure 2)

Most complications occurred infrequently in the study population. The most common surgical complication in our study was Urinary Tract Infection (UTI), in 24 patients (23.3%). Re-exploration of the transplanted kidney wound was done in 19 patients (18.4%), most often for persistent drainage from the wound drain. (Table 2)

Wound related complications (other than lymphocele) were observed in 5.8% of the patients and they accounted for 13.6% of all SCs. Vascular complications occurred in 4 patients, but they were secondary (renal artery thrombosis (RAT) in 2, and partial renal vein thrombosis (RVT) in 2). (Table 2)

The most common medical complication in our study was delayed graft function (DGF) in 23.3%, followed by acute tubular necrosis (ATN) in 20.4%. (Table 4, Figure 3). A relatively higher incidence of ATN was noted in the deceased donor group (80%) and association was found to be statistically significant. (Table 5, Figure 5) Graft nephrectomy had to be done in 2.9% patients.

Overall survival of patients at one year was 86.3%, with one-year survival of grafts of 93.3%. (Figure 4)

## 4. DISCUSSION

KT remains the treatment of choice for ESRD despite the complications and risks associated with the procedure<sup>6</sup>.

### 5.1 Demographic Data

In our study, the number of older age transplant recipients is fewer, and our experience with pediatric transplants (defined as recipients < 18 years of age) is also limited. We had 3 patients under 18 years of age in our study, the youngest was 11 years old. Average age of recipients of KT was 38.8 years. In the study by Levine et al, the average age was 54 years and in the study by Krajewski et al, the average age of KT recipients was 47.8 years<sup>7,8</sup>. Over 75% (76.4%) of the live donors were female in the study group. Mothers and wives were the most common donors in study group.

### 5.2 Medical Complications

The incidence of acute humoral rejection (AHR) in our study was 22.3%. Various studies have shown incidence rates of 5–7% for acute rejection<sup>9</sup>. However, a study from Boston, USA, showed the rates of a single episode of AHR to be 34.9%<sup>10</sup>. A relatively higher incidence of acute humoral rejection was noted in the ABOi group (26.3%) and in the DDK group (50%) of our study.

The incidence of ATN was 20.4%. A relatively higher incidence of ATN was noted in the deceased donor group (80%) and association was found to be statistically significant. The rates in our study compare favorably with the rates in literature<sup>11,12</sup>.

Delayed graft function was seen in 23.3% of patients. This rate compares favorably with the rates in literature<sup>13,14</sup>.

### 5.3 Surgical Complications

The total number of SC's observed was 44 in 35 patients (33.9%). Nine (8.7%) patients had multiple complications while 26 (25.2%) patients developed single surgical complication. Battaglia et al had reported 34.5% rate of surgical complications of KT involving a suboptimal donor<sup>5</sup>. Hernandez et al reported that, within the first 3 months of KT surgery, in low-risk groups involving new immunosuppressive drug regimens, surgical complications were seen in up to 34% of patients<sup>16</sup>. Urological complications are the most common post-KT complications ranging from 3.7 – 14.2% in various case series<sup>17</sup>. Urological complications were seen in 25 (24.3%) patients and they constituted 59% of all surgical complications. However, we have included Urinary Tract Infections (UTI) in this category. UTI was seen in 24 patients (23.3%). No patient developed a urine leak at our centre,

as compared with the rate of 1.5 – 6.0% reported in literature<sup>17</sup>. Ureteric stenosis was seen in 2 (1.94%) patients, which compares well with the expected rate of 0.1 – 12.4%<sup>18</sup>.

Although routine DJ Stenting of the ureteric anastomosis is not done at our centre, primary DJ Stenting was done in patients (n = 23) due to difficult ureteric anastomosis, due to fragile bladder mucosa and as a protocol in DDK. Eleven patients had UTI with DJ Stent in situ (45.8%) and 13 patients had de-novo UTI. On analysis there was a statistically significant association found between UTI and DJ Stenting. Dinckan A et al observed that SC rates in KT recipients with DJ stents were only 5.24%, while in those without DJ Stent was significantly higher at 20%<sup>19</sup>.

Vascular events were seen in 3.8% of patients. Our results are comparable with the published literature, although a longer follow up is required to document the late onset vascular complications, such as renal arterial stenosis (RAS). Aktas et al reported an incidence rate of 2.55% in their analysis of over 1843 patients of which the most common was renal artery stenosis (RAS) occurring in 14 (29.8%)<sup>20</sup>. Haberal et al have mentioned a RAS rate of 0.5 – 0.75 %, and a renal vein thrombosis (RVT) rate of 0.1 – 8.2%<sup>18</sup>. In our study, 1 patient showed suspected RAS on histopathology examination after AHR. Another patient showed suspected RAS after a DTPA scan was done on routine follow-up, but as the patient was progressing well, no intervention was done. RVT was seen in one patient who was in sepsis and in shock, and the RVT was probably due to systemic illness. Another RVT was demonstrated on routine follow-up USG, but on digital subtraction angiography (DSA), it was found to be partial, and was subsequently conservatively managed. We did not see any patient of renal artery thrombosis in our study.

Haemorrhagic complications were seen in 3.8% of the patients. Perirenal haematoma requiring re-exploration and clot evacuation was seen in 4 of our patients (3.8%), but none resulted in graft loss. Pawlicki et al reported an incidence of perirenal haematomas of 25.4%, and a re-exploration rate of 4.5% while studying the influence of disturbed clotting factors on risk for post KT haemorrhage<sup>21</sup>.

Wound related complications (other than lymphocele) were observed in 5.8% of the patients and they accounted for 13.6% of all SC's. Persistent drain discharge and lymphorrhea (defined as drain output > 25 ml/24 hours persisting till post-operative day 7) was seen in 25.2% of patients, however this was not included in the analysis of SC's in our study as this has been shown to be due to allograft and immunosuppressive agents<sup>22</sup>. Lymphocele was seen in 3.8% (n = 4) of patients, accounting for 9% of all SCs. In one patient lymphocele was seen after graft nephrectomy, and it was managed by laparoscopic deroofting. In three other patients, the lymphocele was seen to compress the transplanted ureter causing a rising creatinine level. In all these cases, management was done by open surgery and marsupialization. Haberal et al observed a lymphocele rate of 1 – 40% in various case series<sup>18</sup>. In their study of 108 KT recipients, Fockens et al, reported 8 lymphoceles and 5 wound complications<sup>23</sup>. Two patients (1.9%) had scrotal swelling in our study which were both managed conservatively.

There were also a few patients whose routine post-operative USG showed small peri-nephric collections distributed all around the transplanted kidney but not causing ureteric compression. These collections were managed conservatively and were not included as a surgical complication because of their spontaneous resolution over time.

Graft nephrectomy had to be done in 2.9% patients. In a study by Arvind et al from an Indian centre, the incidence of graft nephrectomy was 4.6%, with early graft nephrectomies, i.e., those done within two months of KT, being 2.7%<sup>24</sup>. Pancreatitis was seen in 1 of our patients (0.9%).

Three patients in the ABO compatible group and 1 patient in DDK group had undergone second transplant. Thirty-three (32.7%) patients in the primary transplant group and 2 (50%) patients in the second transplant group had surgical complications.

### 5.Limitations of the study

Limitations of the study include the single centre nature of the analysis in an experience transplant set-up. This data may not be extrapolated to

newly established centres, who are starting out their KT programme. The sample size is small compared with other recent larger multicenter case series. There is a short follow up period of the patients. Also, there is disproportionate sex ratio with males being in majority so the effect of sex on the incidence of surgical complications could not be assessed accurately.

### 6.CONCLUSIONS

From our study of 103 KT patients we can conclude that surgical complications are more common in patients with diabetes mellitus, and in DDK KT recipients. Immediate surgical complications in our study did not result in death, but long-term morbidity from surgical complications remains a concern in KT patients. Around 93.2% of grafts survived the first year in our study. KT remains a complex procedure with a high incidence of complications even in experienced centers. We intend to add to the growing body of literature of KT surgeries and complications.

### Acknowledgements

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### Author contributions

The research work was primarily done by Author 1. Author 2 participated in the research work and edited the final manuscript. The research work was performed under the supervision and with the participation of Author 3.

### Conflicts of Interest

There are no declared conflicts of interest.

### Complications of Renal Transplant Tables and Figures

**Table 1. Demographic Data**

Demographic Data		
N	103	
Male	76	73.8%
Female	27	26.2%
Diabetic	83 (80%)	
Age, yrs, Mean (SD)	38.8 (13)	
Donor Type		
ABO – compatible (n, %)	74 (71.8%)	
ABO – incompatible (n, %)	19 (18.4%)	
Deceased Donor Kidney (n, %)	10 (9.7%)	
Average duration of stay	22 days	

**Table 2: Surgical Complications**

Surgical Complication	% of patients/103	ABOc/ n=74	ABOi/ n=19	DDK/ n=10
RAT (Secondary)	1.9%	2	0	0
RVT (Partial)	1.9%	1	0	1
UTI	23.3%	11	8	5
DJ Stent	23	14	1	8
UTI with DJS in situ	10.6%	5	1	5
Ureteric Complication	1.9%	2	0	0
Wound Infection (Deb/Sut)	5.8%	3	2	1
Wound Infection (Conservative)	2	2	0	0
Persistent Drain	25.2%	11	12	3
Lymphocele	3.8%	4	0	0
Scrotal Swelling	1.9%	1	1	0
Clot Evacuation	3.8%	4	0	0
Re-exploration	18.4%	14	4	1
Surgical Complications (Patients)	33.9%	22	8	5
Total Surgical Complications (Multiple)	42.7%	27	11	6

**ABOc – ABO blood group compatible**

**ABOi – ABO blood group incompatible**

**DDK – deceased donor kidney**

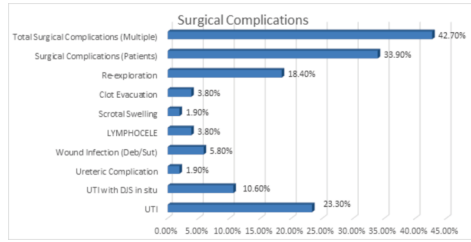


Figure 1: Surgical complications.

Table 3. Complication among each gender

Recipients Gender	ABOc	ABOi	DDK	Total	%	SC's	%
Male	57	15	4	76	73.8%	2+8+16 = 26	59%
Female	17	4	6	27	26.2%	4+3+11 = 18	41%
Total	74	19	10	103		6+11+27 = 44	

ABOc – ABO blood group compatible  
 ABOi – ABO blood group incompatible  
 DDK – deceased donor kidney  
 SC's – surgical complications

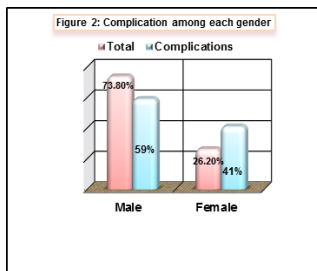
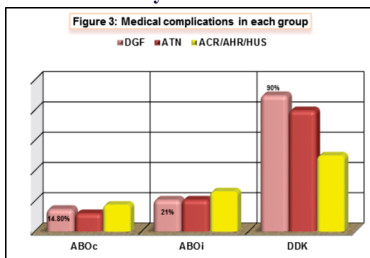


Table 4: Medical Complications

	n/103	%	ABOc/74	%	ABOi/19	%	DDK/10	%
Graft Survival Rate Immediate Post-op	96/103	93.2%	72	97.3%	17	89.5%	7	70%
DGF	24/103	23.3%	11	14.8%	4	21%	9	90%
ATN	21/103	20.4%	9	12%	4	21%	8	80%
ACR/AHR/HUS	23/103	22.3%	13	17.5%	5	26.3%	5	50%
Chest Infection	10/103	9.8%	5	2	2	3	0	
Graft nephrectomy	3/103	2.9%	1	2	0	0		
Second Transplant	4/103	3.9%	3	0	1	1		
1 yr Patient survival	92/103	89.3%	67	90.5%	16	84.2%	6	60%

ABOc – ABO blood group compatible  
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ABOc – ABO blood group compatible  
 ABOi – ABO blood group incompatible  
 DDK – deceased donor kidney  
 DGF – Delayed graft function  
 ATN – acute tubular necrosis  
 ACR/AHR/HUS – acute cellular rejection/acute humoral rejection/hemolytic uremic syndrome

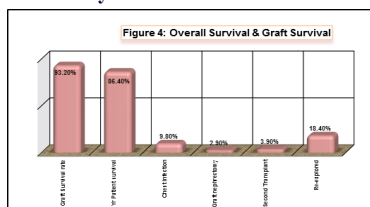
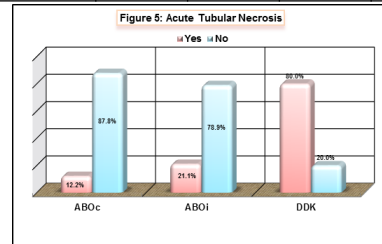


Table 4: Acute Tubular Necrosis

Type of Donor		ATN		Total
		Yes	No	
ABOc	Number	9	65	74
	%	12.2%	87.8%	100.0%
ABOi	Number	4	15	19
	%	21.1%	78.9%	100.0%
DDK	Number	8	2	10
	%	80.0%	20.0%	100.0%
Total	Number	21	82	103
	%	20.4%	79.6%	100.0%
Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	24.983	2	0.000	Sig

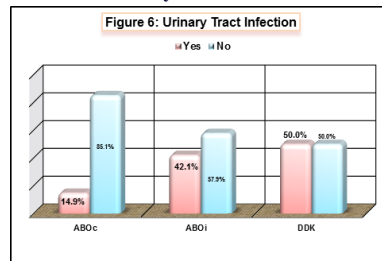


ABOc – ABO blood group compatible  
 ABOi – ABO blood group incompatible  
 DDK – deceased donor kidney

Table 5: Urinary Tract Infection

Type of Donor		UTI		Total
		Yes	No	
ABOc	No.	11	63	74
	%	14.9%	85.1%	100.0%
ABOi	No.	8	11	19
	%	42.1%	57.9%	100.0%
DDK	No.	5	5	10
	%	50.0%	50.0%	100.0%
Total	No.	24	80	103
	%	23.3%	76.7%	100.0%
Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	8.462	2	0.015	Significant

ABOc – ABO blood group compatible  
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