

Original Research

Kidney Transplantation in Nigeria: A Single Centre's Early Surgical Experience and Outcomes

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Academic Editor: Sangil Min

OBM Transplantation

2023, volume 7, issue 2

doi:10.21926/obm.transplant.2302189

Received: March 19, 2023

Accepted: June 07, 2023

Published: June 19, 2023

Abstract

With the rise in the population of patients with End-stage Renal Disease (ESRD) in Nigeria, there is an increased demand for Renal Replacement Therapy (RRT) including kidney transplantation (KT). We present our initial surgical experience and early outcomes with KT at a Nigerian transplant center over 2 years. A 2-year retrospective review of patients who underwent KT was done. Data of both kidney donors and recipients were recorded in designed proformas. Extracted information included demographic characteristics, side of open donor nephrectomy (ODN), recipient anatomy, surgical techniques and postoperative outcomes. Data were analyzed using SPSS version 21. A total of 210 patients had KT during the period



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under review. Donors had an age range of 19 to 53 years with a mean of 30.83 ± 8.43 years while recipients aged between 9 and 73 years with a mean of 45.97 ± 13.71 years. There were 190 (90.5%) male and 20 (9.5%) female donors. One hundred fifty-four recipients were males (73.3%) and 56 (26.7%) were females. Left ODN was performed in 152 (72.4%) of cases and the commonest indication for right ODN was multiple left renal arteries. The allograft was placed in the right iliac fossa in 187 (89.0%) recipients with the external iliac artery preferred for anastomosis with the allograft renal artery in end-to-side fashion in 182 (86.7%) cases. The internal iliac artery was used in end-to-end fashion anastomosis in 28 (13.3%) of cases. Ureteroneocystostomy using the Modified Lich-Gregoir technique over a double-J stent was performed in all but 5 patients who had uretero-ureterostomies. Significant peri-operative hemorrhage necessitating blood transfusion was experienced in 9 donors and 26 recipients. There was a low complication rate in kidney donors. Allograft renal artery thrombosis, venous thrombosis, and arterial pseudo-aneurysms were encountered in 3, 2 and 4 recipients respectively. Kidney transplantation can be safely and routinely carried out in Nigeria. The early surgical outlook of both kidney donors and recipients was found to be excellent in this study.

Keywords

Surgical outcomes; kidney transplantation; end-stage renal disease; Nigeria

1. Introduction

Kidney transplantation (KT) is the most preferred form of renal replacement therapy (RRT) worldwide [1-5]. Following the first reported human kidney transplant by Murray in 1954 between identical twins [6], there have been numerous modifications with a significant improvement in morbidity and mortality rates due to better patient selection, improved surgical techniques, advanced peri-operative care and potent immunosuppressants [7]. Compared to other forms of RRT which include hemodialysis and peritoneal dialysis, kidney transplantation is more cost-effective. It offers the best possible quality of life to patients with end-stage renal disease (ESRD) [2, 3, 8]. With the huge burden of chronic kidney disease in many populations, the need for RRT and a viable KT program has become necessary in many climes.

In Nigeria, a rise in the prevalence of CKD has been reported in the past decade [9, 10] and the attendant challenges associated with the provision of the desired quality of RRT. These inherent challenges include paucity of equipped health facilities, poor health insurance coverage, poverty and ignorance among the populace [2, 8]. When these patients with CKD can access hospitals with facilities for RRT, only a few can afford adequate hemodialysis and a minute fraction can eventually have KT [9]. In the past, only about 10% of patients with ESRD had KT performed in Nigeria [11, 12]. This percentage has likely significantly increased following the birth of privately driven kidney transplant centers in Nigeria [13].

A successful KT program requires a team of multiple specialists including nephrologists, kidney transplants surgeons, anesthesiologists, radiologists, pathologists, specialist renal nurses, dietitians, laboratory scientists, physiotherapists and a modern functional hospital with adequate laboratory

services/support, pharmacies, intensive care units, high dependency units and motivated staff. Following good patient selection and pre-operative preparation, the kidney transplant surgery involves two surgeries occurring almost simultaneously-a donor nephrectomy and kidney implantation in the recipient. A high level of professionalism and experience is required to execute both procedures safely and timely for a good allograft function and successful outcomes in both patients. This paper presents the experience and early surgical outcomes of kidney transplant surgeries carried out at a Nigerian transplant center over 2 years.

2. Materials and Methodology

2.1 Patients

Between January 1st 2019 and December 31st 2020, 210 healthy donors had open donor nephrectomy and the same number of ESRD patients (recipients) had kidney transplantation in our center. All potential donors were seen and evaluated in the outpatient clinic to ensure they met the donor criteria [14]. Individuals <18 years and >60 years were excluded from kidney donation (as per unit protocol). A computerized tomography angiogram was performed on all donors to identify the preferred side for donor nephrectomy [15]. The side with fewer renal arteries and less complex anatomy was commonly selected. The compatibility work-up using the blood group, human leukocyte antigen (HLA), donor-specific antibody (DSA) titers and lymphocyte cross-match were assessed in all patients prepared for KT.

The recipients on the other hand were evaluated for previous abdominal surgeries or renal transplantation, history of recent blood transfusions, femoral venous cannulations and patency of the iliac and femoral blood vessels. Elderly and diabetic patients had routine Doppler ultrasound scans of the iliac vessels to rule out venous thrombosis or significant atherosclerosis which may influence the decision on site for renal transplantation. To forestall qualitative platelet dysfunction and excessive hemorrhage, serum urea and creatinine levels were optimized by scheduling heparin-free hemodialysis sessions before transplant surgery. According to unit protocol, elevated DSA titer above 1000 units had plasmapheresis done at least 48 hours before surgery +/- immunoglobulin administration as required. Ethical approval was obtained from Federal Capital Territory Health Research Committee with approval number: **FHREC/2021/01/158/14-12-21**.

2.2 HLA Antibodies (DSA)

HLA antibody detection method is the Solid phase assay Luminex technology (LABScan 3D); consisting of suspension arrays containing multiple beads containing antigens which are incubated with the recipient's serum (containing the anti-HLA antibodies). A second IgG antibody attached with a fluorochrome is added, creating a fluorescent intensity that is numeric and variable; this is read using lasers through flow cytometry to detect the level of antibodies present and also identify the individual beads. Antibodies detected are directed towards screening for class I and II HLA antibodies; the mean fluorescent intensity (MFI) level is used as a determinant with values higher than 1000 MFI considered as sensitized, and less than that considered not sensitized.

2.3 HLA Typing

This method uses Luminex technology (Luminex-molecular HLA typing: LABScan 3D) which involves sequence-specific oligonucleotides (SSO) probes anchored to microsphere bead (reversed SSO) to identify the HLA alleles present in a PCR amplified product. The presence of HLA alleles is detected by hybridizing the labelled PCR product with microspheres beads, which are identified by lasers, read by Luminex Fusion software, and analysed with Luminex Xponent software.

2.4 Cross Match

Cross-matching is done manually by complement-dependent cytotoxicity (CDC) where the donor's T and B cells are isolated and incubated separately with the recipient's serum. Complement is added to bind to any antibody-antigen complex. To enhance specificity, Dithiothreitol (DTT) is added to break the bonds in IgM (if present which could give a positive result. These cells are stained with vital stains (Fluorescein et al.) to detect cell lysis indicating positivity. This reaction is viewed under fluorescent microscopes in Terasaki plates/wells, with positive reactions appearing Red and negative reactions appearing green.

2.5 Data Analysis

Data of both kidney donors and recipients were recorded on the electronic medical records and inputted into pre-designed proformas. Extracted information included demographic characteristics of patients, details of human leukocyte antigen compatibility, donor-specific antigen titers, details of open donor nephrectomy (ODN), recipient surgery, surgical techniques and post-operative outcomes. The data was analyzed using SPSS version 22 for Windows (SPSS et al., USA). Data results were presented as simple frequencies, percentages, and mean \pm standard deviation.

2.6 Open Donor Nephrectomy Surgery

An extraperitoneal flank approach was used for donor nephrectomy with the operation table in an inverted-V position for all patient (Figure 1). A mini-skin incision measuring between 8 and 12 cm was used via an 11th rib trans-costal approach [16]. The 11th rib was excised to gain better access to the renal hilum especially in right donor nephrectomies. A 6-8 cm length of the ureter was dissected and transected to accompany the renal allograft. At LDN control of the adrenal, gonadal and lumbar veins (when present) is done using either a 300 mm liga-clip or 2/0vicryl sutures. The renal artery and vein are dissected clean at the hilum with enough length to ease anastomosis in the recipient (Figure 2). Ligation of the renal hilar artery and vein were performed using a large polymer hem-o-lock ligation clips or 5/0 prolene sutures especially when a cuff of the inferior vena cava was taken (Figure 3) and silk 0 (artery). The donor nephrectomy team preceded the recipient surgery team by 30 to 45 minutes. The excised kidney was immediately immersed in ice and perfused with 500 mls to 1 L of cold perfusion fluid (0-4°C) till the effluent from the renal vein was clear and devoid of blood. There was no use of drains in the donors.

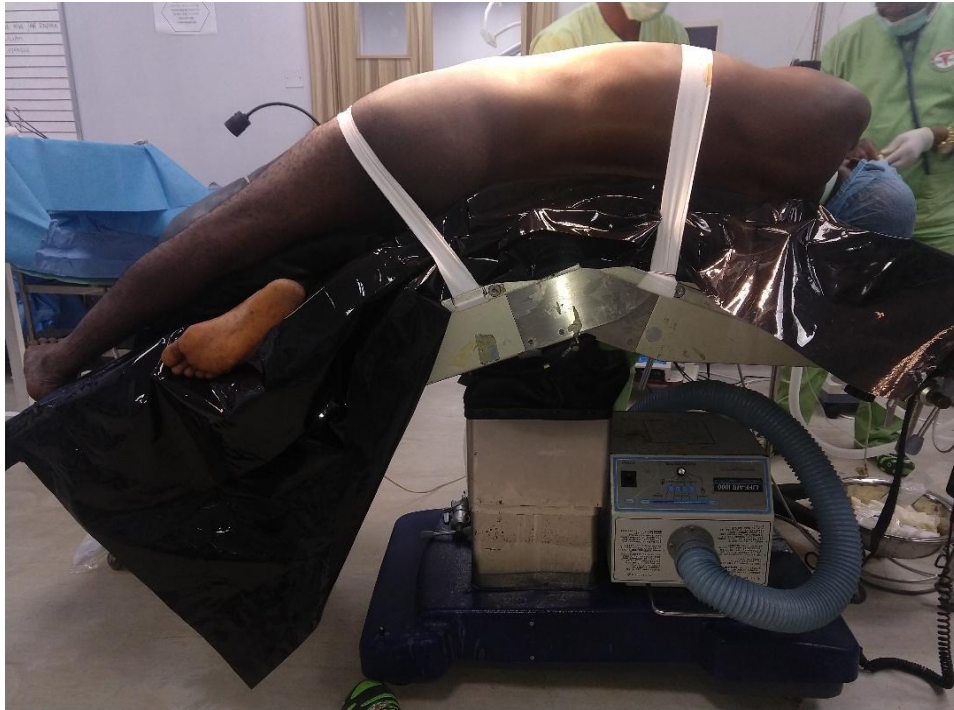


Figure 1 Flank position for Donor Nephrectomy with table in inverted V-formation.

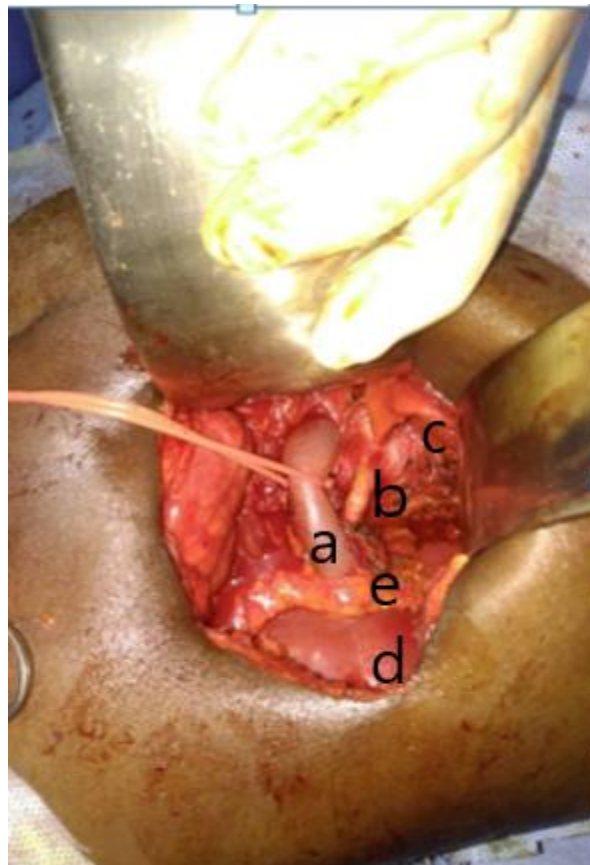


Figure 2 Well dissected left renal hilum in donor nephrectomy with renal vein in red sling. a- Left renal vein, b- left renal artery, c- Abdominal Aorta, d- Left Kidney, e- Perihilar fat.

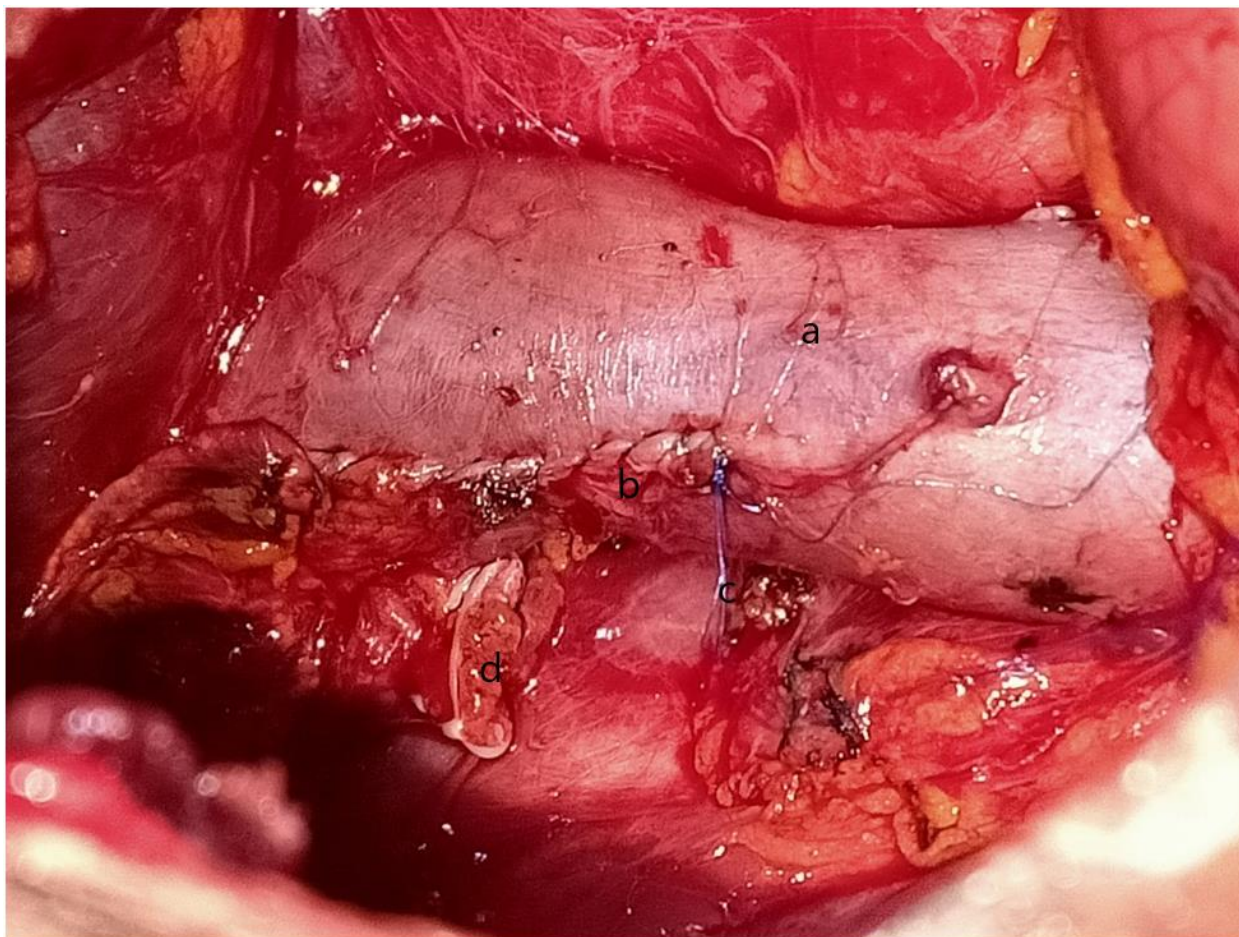


Figure 3 Repaired Inferior vena cava cuff. a- Inferior vena cava (IVC), b- Sutured IVC cuff with Prolene 5/0 Sutures, c- remnant 5/0 prolene suture, d- 2 haem-o-lock clips on the renal artery.

2.7 Kidney Transplantation Surgery

General or regional anesthesia was administered with the patient in the supine position. A Gibson's incision was made and deepened in a complete extra-peritoneal fashion to gain access to the iliac group of vessels and the ipsilateral ureter. The external iliac artery and vein were dissected and mobilized to allow for an easy, tension-free anastomosis. A book-water self-retaining retractor enables excellent exposure during anastomosis of the renal allograft artery and vein to the iliac vessels as well as the ureteroneocystostomy/uretero-ureterostomy (Figure 4). Specialized instruments like the Potts' vascular scissors, vascular punch, ring-tip forceps, debakeys dissecting forceps and vascular clamps make surgery relatively easier. Vascular anastomoses were carried out using proven 5/0 or 6/0 sutures using the external or internal iliac artery or vein. Ureteroneocystostomy was done using PDS4/) sutures with the modified Lich Gregoir technique or uretero-ureterostomy with double J stents and wound drains inserted in all patients.

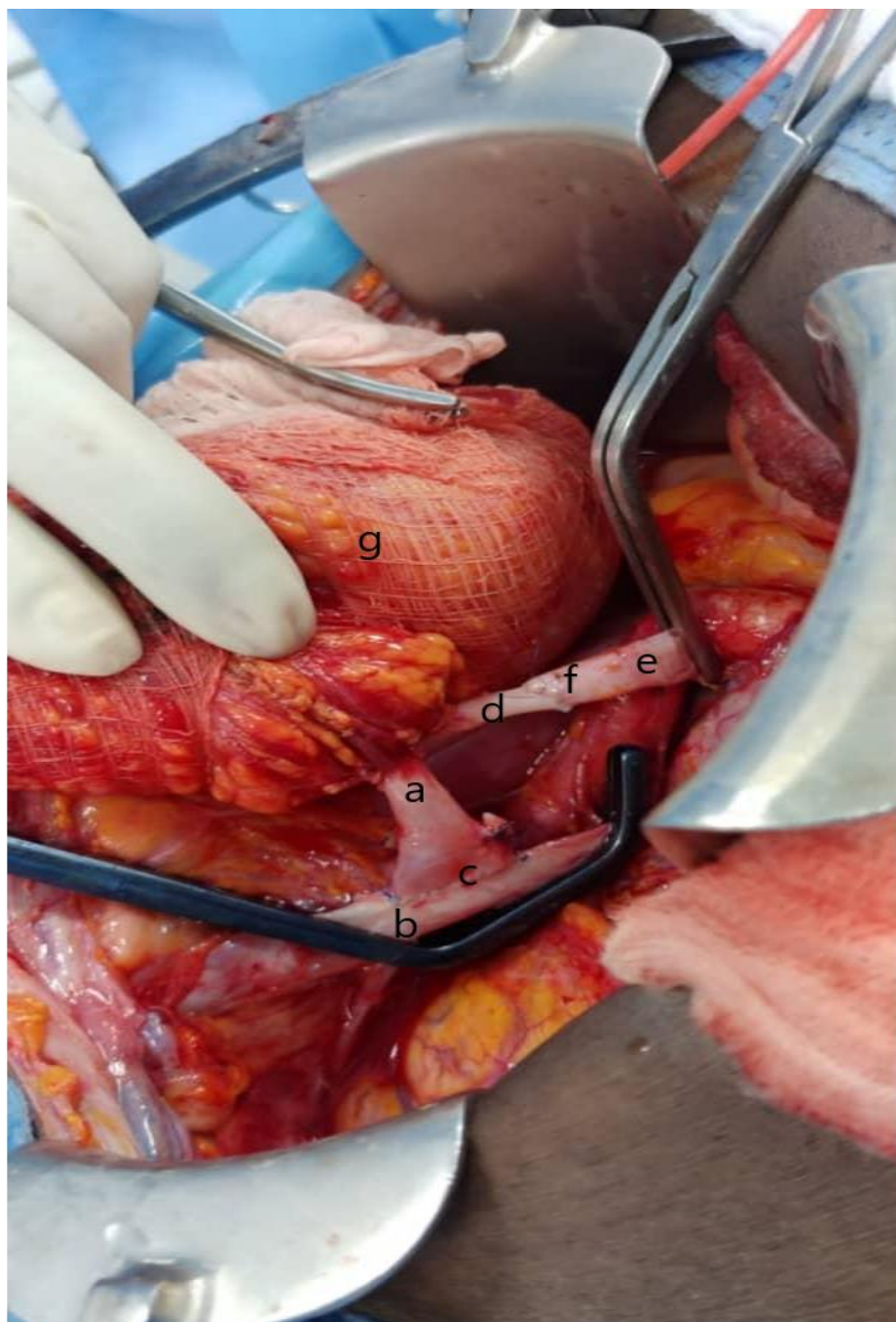


Figure 4 Vascular anastomosis of Renal Allograft before perfusion. a- Allograft renal vein, b- External Iliac vein, c-anastomosis in end-to-side fashion, d- Allograft renal artery, e- Internal Iliac Artery, f- Anastomosis in end-to-end fashion.

3. Results

A total of 210 patients had KT during the 2-year period under review. A total of 99 cases were performed in 2019 and 111 in 2020 amidst the COVID-19 pandemic. Donors had an age range of 19 to 53 years with a mean of 30.83 ± 8.43 years while recipients aged between 9 and 73 years with a mean of 45.97 ± 13.71 years. Other characteristics of the donors are depicted in Table 1. Recipient demographics are also depicted in Table 2. Left open donor nephrectomy (ODN) was performed in 152 (72.4%) cases while 58 (27.5%) were on the right. The commonest indication for right ODN was

multiple left renal arteries. All ODN surgeries were approached via the flank through either an 11th rib transcostal or subcostal incision. Of the 58 patients who had right ODN, 40 had 11th rib transcostal incision with resection of the 11th rib for better access to the renal hilum. The duration for donor nephrectomies ranged from 72-200 minutes with a mean duration of 130 ± 28 minutes and the length of flank incisions ranged from 8-15 cm with a mean incision length of 11.8 ± 2.0 cm.

Table 1 Donor characteristics and Complications.

Variable		Frequency	Percentage(%)
Age (years)	11-20	6	2.9
	21-30	132	62.9
	31-40	59	28.1
	41-50	12	5.7
	51-60	1	0.4
	Mean \pm SD	30.83 ± 8.43	
	Range (Min, Max)	34 (19, 53)	
Sex	Male	190	90.5
	Female	20	9.5
Side of Nephrectomy	Right	58	27.6
	Left	152	72.4
	Mean \pm SD	106.41 ± 42.50	
First warm Ischemic time (In seconds)	Median	110.00	
	Range (Min, Max)	200 (25, 225)	
	Mean \pm SD	33.26 ± 20.01	
Cold ischemic time (In minutes)	Median	39.00	
	Range (Min, Max)	62 (11, 72)	
	Mean \pm SD	40.05 ± 13.81	
Second warm ischemic time (In minutes)	Median	49.00	
	Range (Min, Max)	43 (18, 65)	
	Excessive		
Complications	primary haemorrhage	9	4.2
	Pleural injury	4	1.9
	Peritoneal breach	12	5.7
	Surgical site infection (Figure 5)	6	2.9
	Peri-operative mortality	0	0



Figure 5 Superficial Surgical Site infection in a donor.

Table 2 Recipient Characteristics and Complications.

Variable		Frequency	Percentage
Age (years)	11-20	8	3.8
	21-30	11	5.2
	31-40	34	16.2
	41-50	53	25.2
	51-60	59	28.1
	61-70	40	19.1
	71-80	5	2.4
	TOTAL	210	100
	Mean \pm SD	45.97 \pm 13.71	
Sex	Range (Min, Max)	64 (9, 73)	
	Male	154	73.3
	Female	56	26.7
Side of Surgery	Right	187	89.1
	Left	23	10.9

Complications	Acute tubular necrosis/delayed graft function	16	5.7
	Acute Allograft Rejection	24	11.4
	Allograft renal artery thrombosis	3	1.4
	Allograft renal vein thrombosis	2	0.95
	Allograft renal artery stenosis	3	1.4
	Peri-operative haemorrhage	26	12.4
	Allograft rupture	2	0.95
	Renal artery Pseudo-aneurysm (Figure 6)	4	1.9
	Retained wound drain	2	0.95
	Surgical site infection (Figure 7)	8	3.8
	Urine leak (Figure 8)	5	2.4
	Ureteric stenosis	2	0.95
	Retained double J stent	2	0.95



Figure 6 Computerized Tomography Angiogram showing Left Renal Allograft Artery Pseudo-aneurysm with infarction of Allograft. a- Abdominal Aorta, b- common iliac artery, c- left External Iliac Artery, d- left internal iliac artery, e- Pseudo-aneurysm obstructing arterial blood flow into the renal allograft, f- Position of infarcted renal allograft, g- left femoral artery.



Figure 7 Surgical site infection in a Kidney transplant Recipient.

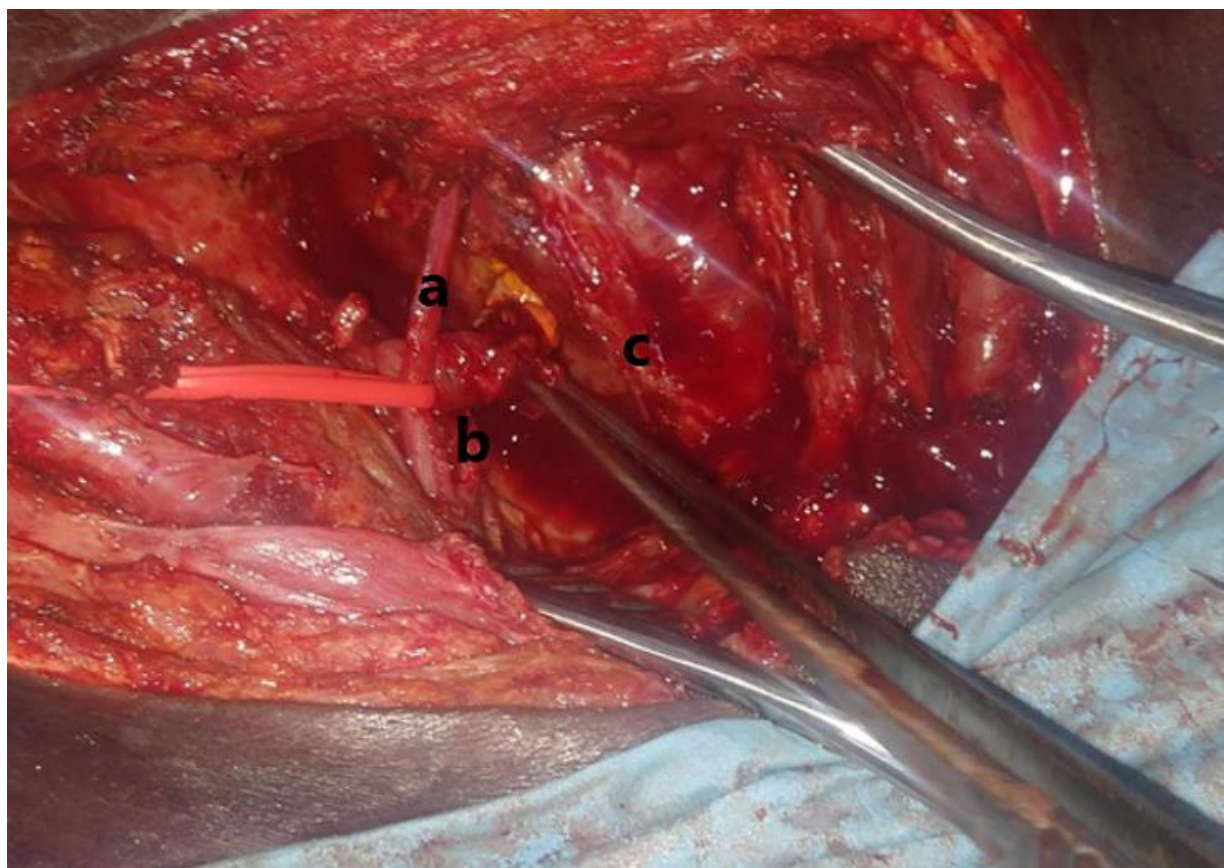


Figure 8 Necrotic edge of the Ureter in Post-transplant patient with Urine leak. a- Spermatic cord, b- Allograft ureter with forcep showing the necrotic edge, c- Urinary bladder.

The recipients were placed supine and had a Gibson incision. Following an extra-peritoneal preparation of the bed, the renal allograft was placed in the right iliac fossa in 187 (89.0%) patients with the external iliac artery preferred for anastomosis with the renal allograft artery in end-to-side fashion in 182 (86.7%) cases. The internal iliac artery was used in end-to-end fashion anastomosis in 28 (13.3%) cases. Similarly, the external iliac vein was anastomosed with the renal allograft vein in 206 (98.1%) cases. The common iliac vein [3] and inferior vena cava [1] were used in the remaining 4 cases. The 1st warm ischemic time ranged from 25 to 225 seconds with a mean of 106.41 ± 42.50 seconds. The cold ischemic time ranged from 11 to 72 minutes with a mean duration 33.26 ± 20.01 minutes. The second warm ischemic time ranged from 18 to 65 minutes with a mean duration of 40.05 ± 13.81 minutes.

Ureteroneocystostomy using the Modified Lich-Gregoir technique over a double-J stent was performed in all but 5 patients who had uretero-ureterostomies and the stents removed following 4 weeks of surgery as per unit protocol [17, 18]. Delayed removal of double-J stents beyond 4 weeks was encountered in 12 patients with complications like urine leaks in the post-operative period. Significant peri-operative hemorrhage necessitating blood transfusion was experienced in 9 (4.2%) kidney donors and 26 (12.4%) recipients. Renal allograft nephrectomy following various complications was performed in 14 (6.7%) patients.

4. Discussion

Before now, patients with ESRD in Nigeria had limited options for RRT. A significant percentage succumb to the disease following a few hemodialysis sessions, which they could only sustain for a few months [2]. The paucity of centers in sub-Saharan Africa with the expertise for KT has further worsened the outlook for these patients. In the past two decades, a significant percentage of Nigerian patients have traveled abroad to have their KT done and subsequently struggled to sustain follow-up care, a trend that is gradually changing with the growth of privately-owned Nigerian kidney transplant centers [11].

The mean age of living kidney donors in this study of 30.83 ± 8.43 years was comparable to values reported in Ethiopia's pioneering KT center [19]. In contrast to other studies with more female than male donors [19-21], we found a significantly higher population of male donors. The recipients on the other hand had a mean age of 45.97 ± 13.71 years which was comparable to findings by Umezurike in Nigeria [11]. There appears to be a higher population of male than female recipients in literature as was found in this study [19].

All kidney donors were evaluated for compatibility and had high-quality CT angiography to assess and determine the vascular anatomy of the kidneys and decide on which was most suitable for donor nephrectomy [15, 22]. Donor nephrectomies were performed in an open fashion in this study for all patients, in contrast to the developed world where laparoscopic hand-assisted and robotic nephrectomies are the standard of practice [16, 19, 21, 22]. Left open donor nephrectomy was more commonly performed in this series in a ratio 4:1, similar in literature [23, 24] due to the longer left renal vein and its convenience during anastomosis.

The renal allograft was most commonly transplanted in the right iliac fossa in our practice due to the more conveniently superficially placed external iliac vessels, making anastomosis easier as reported in other studies [7].

The first warm ischemic time in this study was 106.41 ± 42.50 seconds, this is comparable with results from a transplant center in Egypt with FWIT of 126 ± 24 seconds [25], but significantly lower than 394 seconds reported by Nugroho *et al.* in a single center report in Indonesia [26]. This study's cold ischemic time of 33.26 ± 20.01 minutes is significantly shorter than majority of transplant programs worldwide. However, it has been proven that CIT less than 12 hours may not significantly worsen allograft function and outcomes [27, 28]. This CIT is, however, significantly higher than the 8:04 minutes reported by Nugroho *et al.* [26]. Some factors in our series that affect CIT duration include renal allograft perfusion, bench dissection, ligation of potentially hemorrhagic blood vessels and occasional anastomosis of multiple renal arteries. Additionally, this study's second warm ischemic time is comparable to those reported in similar settings [29, 30]. Longer Ischemic time is associated with poor early graft function and renal transplant outcomes [26, 27, 29-32]. Ischemia is a trigger of noxious agents in the graft, the effects of these agents are amplified when the blood supply reperfusion is restored, giving rise to inflammatory and immune responses in kidney grafts [32]. The acceptable ischemic time in our experience has significantly impacted successful outcomes with a very low prevalence of DGF.

The prevalence of complications in the donors following surgery was 14.7%, out of which peritoneal breaches were 5.7%, hemorrhage: was 4.2% and surgical site infection: was 2.9%. A national study by Lentine *et al.* in 2016 determined the national prevalence of donor complications following surgery in the United States at 16.8%, with the most common being gastrointestinal (4.4%),

hemorrhage (3.0%) and respiratory (2.4%) [33]. In another study by Van der Merwe & Heyns among 50 South Africans, the prevalence of complications was 10%, out of which renal vein reconstruction was 4%, and infection, urethral injury and acute gastritis were all 2% [34]. Meanwhile a 4-year retrospective study in Kenyatta National Hospital reported the prevalence of donor complication to be 7.14%, the distribution being pleural breach (3.57%), hemorrhage (2.38%) and peritoneal breach (1.19%) [35]. Factors significantly associated with increased risk of donor complications following nephrectomy are African-American race, hematologic and psychiatric conditions, older age, obesity, and pre-donation hypertension [33, 36, 37].

The commonest complication for the recipients in our study was peri-operative hemorrhage (12.4%), acute allograft rejection (11.4%) and delayed graft function (5.7%); others are surgical site infection (3.8%), urine leak (2.4%) and thromboembolic events (2.4%). These results are not far from reports by Arogundade in a 10-year review where the prevalence of acute rejection was between 15-30% [2]. These results are also in tandem with some of the findings by Davidson *et al.* in South Africa, where the incidence of acute allograft rejection is 16.6%, surgical site infection is 2.5%. However, they reported a significantly higher incidence for delayed graft function (21.4%), thromboembolic events (6.2%), and urine leak (5.2%) [38]. Some differences in these findings are also reported in Senegal by Berhe *et al.*, surgical site infections are more prevalent (7.6%), and graft loss is less prevalent (1.9%) [39]. Surgical complications associated with kidney transplantation can occur at any time and significantly impact recipient and graft survival. Adhering strictly to standard surgical techniques and ongoing research to develop novel and better techniques can help improve the surgical experience of kidney transplant recipients.

Some of the limitations of this study include the fact that it is a retrospective and single-centered study. In the future, a prospective, multi-centered study with 1, 5 and 10-year graft and host survival data will need to be incorporated to advance the knowledge on kidney transplantation in the African sub-region.

5. Conclusion

There has been rapidly increasing experience in kidney transplantation in Nigeria over the past few years. The early surgical outcomes are comparable to best practices globally. A low prevalence of post-operative complications in both donors and recipients was found in this study. This report suggests kidney transplantation can be successfully and safely performed in Nigeria. There is a need for long-term follow-up of the patients to ascertain graft survival, mortality and other outcomes in the future.

Acknowledgments

We acknowledge the entire staff of ZMKC for the support during the execution of this study.

Author Contributions

The authors contributed equally to the writing of the manuscript.

Competing Interests

The authors declare no conflict of interest.

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