

# Kidney transplantation in a low-resource setting: Nigeria experience

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The incidence and prevalence of chronic kidney disease and end-stage renal disease (ESRD) have continued to increase exponentially all over the world in both developed and developing countries. While the majority of patients in developed countries benefit from various modalities of renal replacement therapies, those from developing economies suffer untimely deaths from uremia and cardiovascular disease. Kidney transplantation (KT) leads to improvement in both the quantity and quality of life. Unfortunately, it is not exploited to its full potential in most countries and this is particularly the case in developing economies. Only a very small fraction of the ESRD population in emerging countries ever gets transplanted because of the many constraints. This review focuses on KT in Nigeria between 2000 and 2010 and assessed particular challenges that need be addressed for KT potential to be fully harnessed in such resource-constrained settings. A total of 143 KTs were performed in 5 transplant centers, some of which have only recently opened. One-year graft and patient survival was 83.2% and 90.2%, respectively, while the 5-year graft and patient survival was 58.7% and 73.4%, respectively. Mortality was reported in 38 (27%) of recipients. The complications recorded included acute rejection episodes in 15–30%, chronic allograft nephropathy in 21 (14.7%) and malignancies, particularly Kaposi Sarcoma, which was reported in 8 (5.6%) recipients. It was concluded that KT has led to an improved survival but is bedevilled with unaffordability, inaccessibility, a shortage of donor organs and poor legislative support. Enactment of relevant organ transplant legislation, subsidization of renal care, and further development of local capacities would improve KT utilization and thus lead to better outcomes.

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## INTRODUCTION

Kidney transplantation (KT) remains the gold standard renal replacement therapy, as it not only corrects renal functional impairment but also provides excellent or near normal quality of life for recipients and is the most cost-effective therapy.<sup>1–4</sup> This is especially the case for sub-Saharan Africa, where maintenance dialysis is beyond the reach of most of the population.

Nigeria is the most populous black nation in the world with an estimated population of 158.4 million. It is located in West Africa, with a surface area of 910,770 km<sup>2</sup>. It has a literacy rate of 61% and average life expectancy of 51 years.<sup>5</sup> The gross national income per capita was \$1180 in 2010.<sup>5</sup>

Chronic kidney disease (CKD) prevalence is high in Nigeria and is found in 16 and 26% of the population in community studies.<sup>6–8</sup> CKD diagnosis in such studies was based on persistent proteinuria or reduced glomerular filtration rate or both.<sup>6–8</sup> On the other hand, ESRD prevalence reported in some community studies ranges between 0 and 1%, but constitutes 6.7–8.4% of medical admissions in different hospital reports throughout the country.<sup>9,10</sup> We have observed an exponential increase in the ESRD admission rates over a 19-year period in our hospital (Figure 1).<sup>9</sup> The causes of CKD in Nigeria, as in many other African countries, are hypertension and chronic glomerulonephritis. Diabetic nephropathy (DN) ranks a distant third, although a rising prevalence has been observed in different countries within sub-Saharan Africa.<sup>10–13</sup> In many instances, the cause may be unclear because of the advanced nature of the CKD.<sup>10–13</sup> It has also been found that CKD and ESRD patients present at a relatively young age usually between 20 and 50 years when compared with those from the developed world.<sup>9,13</sup> This is probably because of the preponderance of infection-related chronic glomerulonephritis and the predisposition of blacks to hypertensive renal damage. The effect of genetic susceptibility is increasingly being recognized, particularly, the polymorphisms in *MYH 9* and *APOL 1* genes.<sup>14–16</sup> Studies have also reported a significant male preponderance in different parts of sub-Saharan Africa.<sup>9–13</sup>

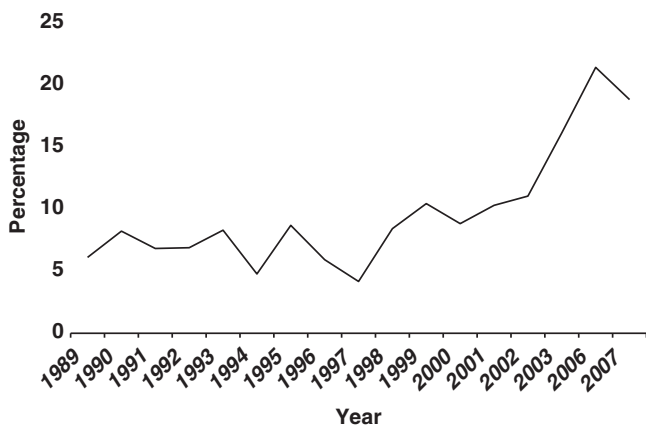
The management of end-stage renal disease (ESRD) in Nigeria as in many parts of the world is costly, especially as in our setting, individual patients are directly financially responsible for their care, government subsidy is virtually nonexistent, and renal care is still not covered by the national

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health insurance scheme. Thus, the outcome is a very high mortality rate with about 80% of ESRD patients dying within a few weeks of diagnosis.<sup>9,17,18</sup> In our center, hemodialysis remains the most commonly prescribed renal replacement modality in 70% cases, though only 5% of the patients are able to sustain the treatment for longer than 12 weeks, mainly because of these financial constraints. Continuous ambulatory peritoneal dialysis has been offered in only 1.2% and KT in just 1% of our patients.<sup>9,19,20</sup> Of note, are the superior survival figures observed in our CAPD and transplanted patients. Major constraints to CAPD use included unavailability and unaffordability of consumables and high infection rates.<sup>19</sup> This contrasts with the global renal replacement therapy utilization figures reported by Grassman *et al.*,<sup>20</sup> where hemodialysis was used in 68% of ESRD patients, Kidney transplant in 23% and CAPD in only 8%. KT is recognized globally as the gold standard treatment modality for ESRD patients because of its overall cost effectiveness, guaranteeing of an almost normal quality of life, as it affects different domains and reduced frequency of hospital visits and hospitalizations.<sup>1-4,13</sup> It however has its constraints, which include the huge financial outlay at the outset, shortage of donor organs, challenges of immunosuppression and, very recently, organ trafficking<sup>13,21-28</sup>. This current review is aimed at assessing kidney transplant activities in Nigeria from the years 2000–2010 with the objective of highlighting the outcomes and challenges. This is to be able to proffer ethically and culturally acceptable solutions to the identified challenges without compromising standards.

**RESULTS**

One-hundred and forty-three (143) kidney transplants were performed in Nigeria with 70% of these taking place in the private sector (Figure 2). There were 110 males and 33 females. It included two pediatric transplantations and three second transplants. Only living donation was practiced as cadaveric donation is still not available. The majority of donors (118/82.5%) were genetically related, while the remaining 25 (17.5%) were emotionally related. Genetically



**Figure 1 | End-stage renal disease (ESRD) patients as percentage of medical admissions in Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria.**

related donors are usually first-degree relatives (siblings, parents or children) or first cousins. Tissue typing was performed abroad for all the patients. The choice of tissue-typing centers varies between institutions but included United Kingdom, Egypt, South Africa, and Sudan.

**Funding of KT in Nigeria**

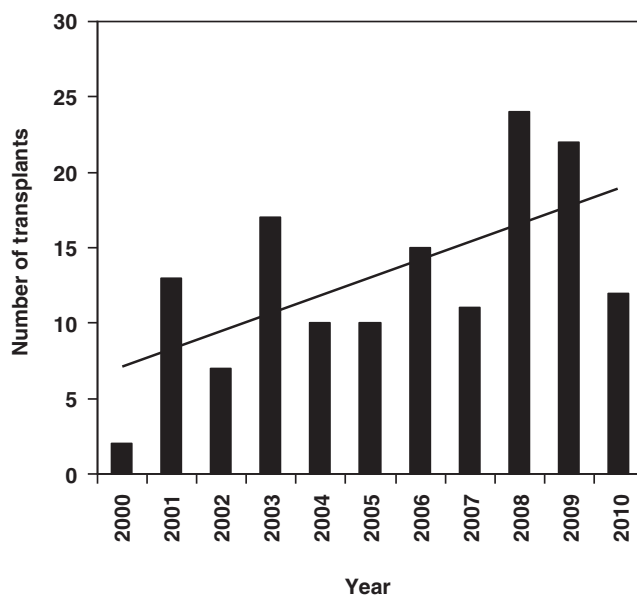
Funding of kidney transplant preparation and surgery is borne by patients or relations in about half of the population, while in the other half, funds are sourced from employers, government donation, philanthropists etc. However, the funding of maintenance therapy is usually borne by patients in 75% of cases (Table 1).

**Immunosuppressive regime**

Immunosuppressive regimes used included Calcineurin inhibitor-based triple drug therapy as induction and maintenance regimes in 137 (95.8%) recipients, while antibody induction therapy was used in 6 (4.2%) recipients.

**Transplant outcome**

One-year graft and patient survival ranges between 75% and 100% in different centers, while the 5-year graft and patient



**Figure 2 | Kidney transplantation in Nigeria (2000–2010).**

**Table 1 | Funding of kidney transplant management in Nigeria**

Sources	Transplant surgery	Maintenance therapy
Private/personal	48 (33.6%)	107 (74.8%)
Employer	34 (23.8%)	34 (23.8%)
Philanthropists	13 (9.1%)	Nil (0%)
Other donations	31 (21.7%)	Nil (0%)
NGO	2 (1.4%)	2 (1.4%)
Governmental support	15 (10.5%) (AD-HOC)	Nil (0%)
Health insurance	Nil (0%)	Nil (0%)

Abbreviation: NGO, non-governmental organizations.

survival range between 55% and 70%. Overall, 1-year graft and patient survival was 83.2% and 90.2%, respectively, while the 5-year graft and patient survival was 58.7% and 73.4%, respectively.

A total of 38 (27%) recipients died. Causes of deaths included Cytomegalovirus infection and septicemia in 26 (68.4%) of the deaths, cardiovascular disease in 6 (15.7%), graft failure in 3 (7.8%), malignancies in 2 (5.2%), and unknown in 1 (2.6%).

### Complications

The complications reported from the different centers included acute rejection episodes (ARE) in 15–30% of recipients. Steroid-resistant rejection has been recorded in only 5 (3.5%) recipients.

Chronic allograft nephropathy (CAN) was reported in 21 (14.7%) patients and many have recommenced maintenance hemodialysis, with only 3 securing a second kidney transplant.

CMV infection is common, as over 90% of our recipients are CMV IgG positive at transplantation. Malignancies have been reported in our KT recipients, Kaposi Sarcoma was reported in 8 (5.6%) recipients, while lymphoproliferative disease and Pancreatic malignancy was seen in 1 (0.7%) recipient each.

### DISCUSSION

KT was first undertaken in March 2000 in a private hospital in Lagos (St Nicholas Hospital), with another two units (in Ile-Ife and Kano) starting 2 years later.<sup>21,22</sup> As at time of this review, five units have carried out KT in Nigeria though cumulative transplant activity is less than 50 transplants per year. Only living and emotionally related KT are available in Nigeria. Deceased organ donation is not available, principally because of the lack of enabling legislation and logistic support. Pediatric transplantation, which is available only in one center, was introduced in 2009.

### Donor sourcing

As there is no cadaveric transplantation only living donation has been practiced. The majority of donors (118/82.5%) are genetically related while the remaining 25 (17.5%) are emotionally related. An independent ethical committee in each of the transplant centers ensures the altruism of emotional donors and, where necessary, legal authorization is sought. This is to ensure that commercialism is prevented and that there is strict adherence to the Declaration of Istanbul.<sup>23,24</sup> Suitability for donation is determined by the results of HLA typing and crossmatching, and assessment of donor-specific antibody or panel-reactive antibodies as well as serological screening. Tissue typing was outsourced abroad and was initially by ELISA, but has since been replaced by molecular techniques (PCR). A matching of 50% or higher at A, B, and DR loci are generally acceptable. Individuals that are Hepatitis B virus or Hepatitis C virus (HCV) positive or HIV positive are not generally accepted in Nigerian programs at this time.

### Recipient preparation

Good control of hypertension, a normal glycaemic profile and overall normal cardiovascular status are prerequisites. As pre-emptive transplantation is not commonly performed in our centers, recipients must be adequately dialysed and the hemoglobin profile must be maintained within acceptable limits (usually greater than or equal to 11 g/dl). As with donors, positive Hepatitis B serology or HCV and HIV-positive patients are not generally accepted in Nigerian programs except after HCV has been successfully treated and eradicated. As of this time, none of the transplant centers perform KT for HIV-positive recipients. All the transplant centers are adequately equipped to investigate donors and recipients in preparation for KT. However, HLA typing is still not well established locally, hence the reliance on centers abroad.<sup>21,22,25</sup>

### Immunosuppressive regime

All the centers use calcineurin-based triple drug induction regimes comprising Cyclosporin or Tacrolimus in combination with Azathioprine or Mycophenolate mofetil (MMF) and Prednisolone. These regimes were used in 137 (95.8%) recipients, while antibody induction therapy has been used in 6 (4.2%) recipients, which included pediatric patients and second transplants and presensitized recipients.

For maintenance immunosuppression, a calcineurin-based triple drug regime has been used in all the patients. Steroid-free immunosuppression is rare and sirolimus was only used in patients who developed complications, particularly malignancies (Kaposi Sarcoma). Cost-saving immunosuppressive regimes utilizing ketoconazole or diltiazem are rarely used.<sup>26</sup>

### Transplant outcome

One-year graft and patient survival figures are similar to those recently reported in African Americans but are considerably lower than figures reported in white Americans or Europeans. Genetic differences may have a major role, as the baseline characteristics were not found to significantly influence long-term survival.<sup>28</sup> A total of 38 (26.5%) recipients had died, Cytomegalovirus infection and septicemia were responsible for more than half of the deaths recorded, whereas cardiovascular diseases, malignancies, and graft failure were responsible in some of the patients.

### Complications of KT

ARE have been reported in up to a third of the recipients in some centers but are usually steroid responsive. Steroid-resistant rejection has been recorded in only 5 (3.5%) recipients. AREs were usually suspected on clinical grounds but confirmed by histology using Banff criteria.<sup>29</sup>

CAN was reported in 21 (14.7%) patients and many have recommenced maintenance hemodialysis, with only 3 securing a second kidney transplant.

CMV infection is common as most of our recipients are CMV IgG positive at transplantation. Some of the centers

now give acyclovir prophylaxis but ganciclovir and valganciclovir are relatively unavailable locally. Post-transplant diabetes mellitus and worsening of glycemic control in diabetic nephropathy patients has been observed in a few patients.

Malignancies have also been seen in our KT recipients with Kaposi Sarcoma being the commonest.<sup>30</sup> It was reported in 8 (5.6%) recipients, while lymphoproliferative disease was reported in only 1 (0.7%) recipient. Of special note is the regression of Kaposi Sarcoma with adjustment of immunosuppressive regime, which included withdrawal of cyclosporine, introduction of Sirolimus or Mycophenolate mofetil (MMF) with or without adjuvant chemotherapy (vincristine) and/or radiotherapy. A pancreatic malignancy has been reported in one patient.<sup>25,30</sup>

### Challenges of KT in Nigeria

Funding of KT remains a major challenge as the majority of patients are poor, hence the procedure is unaffordable and therefore inaccessible to the majority of them.<sup>25,26</sup>

In a number of instances, donor shortage is another important factor as available relatives or spouses may be unsuitable or unwilling to donate. The development of cadaveric donation would assist in alleviating this quandary, but would provide a major technological challenge.

Tissue typing/crossmatching as well as some viral studies, which are major aspects of patient preparation, are usually conducted overseas. This tends to delay the procedure and leads to an increase in the cost. The development of local tissue-typing laboratories would not only reduce cost but also save the much needed time spent on transporting samples abroad.

Drug monitoring (assays) are also currently only irregularly available locally with the result that samples are also sent abroad. This leads to frustrating delays in optimizing treatment. Development of local capacities, which has been introduced in three centers, needs to be exploited to its full potential.

Antiviral drugs and induction agents are also imported when needed. Their unavailability may have contributed to the mortalities recorded from CMV infection.

Even though the necessary medical and surgical expertise required for establishing transplant programmes are available in many centers, the relatively low transplant activity may be counterproductive on the whole. It may be desirable because of the size of the country and other socio-political considerations, to establish only three national transplant centers that will freely collaborate, and where expertise could be concentrated. This would in the long term lead to better exposure of the trained personnel and culminate in improvement in transplant activities and outcomes. It would also further enhance transplant research and training.

The recommendations on the special requirements for transplantation in emerging countries as well as guiding principles on ways of ensuring best practices, improved utilization and better outcomes in KT as documented in the

outcomes from the Bamako meeting and WHO guiding principles, would assist in optimizing the benefits of KT in emerging countries, including Nigeria.<sup>31</sup>

### Conclusion

KT practice has improved in Nigeria. It has led to improved survival of ESRD patients. However, funding and availability of donors are major limiting factors, while laboratory support needs to be further improved. Enhanced coverage of renal care by insurance (national health insurance scheme) should improve accessibility. It is necessary to hasten the process of enactment of relevant kidney transplant legislation in Nigeria in conjunction with the Declaration of Istanbul to increase the transplantation rate, but also to prevent commercialism and organ trafficking. Establishment of only three national transplant centers would improve exposure of patients to trained personnel and prevent a proliferation of smaller units, which may be counterproductive.

### METHODS

A questionnaire was designed and electronically mailed to Nephrologists in all transplant centers in Nigeria. Information sought included number of kidney transplants performed between January 2000 and December 2010, donor sourcing, tissue-typing availability, patient and graft survival, immunosuppressive regimen, complications observed including acute and chronic rejections, mortality as well as causes of deaths etc. Data collated was analyzed using descriptive statistics.

### DISCLOSURE

The author declared no competing interests.

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