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Transplant: The Success of Renal Transplant Programs



Ebun L. Bamgboye, MBBS, FWACP, FRCP, FNAN*

Manjusha Yadla, MBBS, MD, DM, MISN, FISN[†] Guillermo Garcia-Garcia, MD, FACP[‡]

Vincent Boima, MBChB, FWACP, FGCP, MPH, Cert Nephrology (SA)[§]

Privilage D. Makanda-Charambira, MBChB (Zim), Mmed Paeds (Zim), DCH (Aus), Cert Paed nephrology (SA), MPhil Paed Nephrology (SA), Fellow ISN/IPNA^{||}

Mignon I. McCulloch, MBBCh (Wits), DCH (SA), DTM&H (UK), FRCPCH (Lon), FCP Paeds (SA)[¶] and Dwomoa Adu, MD, FRCP[§]

Summary

In the absence of malignancy or other severe comorbidity, kidney transplantation offers better survival rates and quality of life than dialysis. Despite this survival advantage, many lower- and upper-middle-income countries do not offer adequate kidney transplant services. This is particularly troubling because end-stage kidney disease often is more common in these countries than in high-income countries and overall is less costly in the life of a patient. We describe the contrasting levels of provision of kidney transplantation in Mexico, India, Nigeria, Ghana, and Zimbabwe, and kidney transplant services for children in Africa.

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Chronic kidney disease is common worldwide, but the use of kidney replacement treatment (KRT) is limited in most low-income and middle-income countries. The extent of KRT correlates with income, and it is estimated that there are 1.2 million premature deaths per year owing to a lack of access to kidney replacement therapy.¹ In most countries the major modality of treatment is hemodialysis,¹ although survival and quality of life are better with a kidney transplant than with ongoing dialysis.^{2,3}

AFRICA

In Africa, countries with a high level of transplantation are Tunisia, South Africa, Sudan, Algeria, Egypt, and Morocco. Currently, there are 8 countries in sub-Saharan Africa where

successful kidney transplants are performed.⁴ The estimated number of transplants performed, the dates when the first transplant was performed, the average number of transplants performed in the past 3 years, and the number of transplant centers available in each of these countries are described in Table 1. The majority of these countries perform live-donor (LD) kidney transplants exclusively, and in Africa only Morocco, Algeria, Tunisia, and South Africa have a deceased donor (DD) kidney transplant program. Setting up a kidney transplantation service requires substantial infrastructure in addition to surgical, medical, nursing, and anesthetic skills, and a major barrier is the cost of immunosuppression.⁵ Additional barriers to kidney transplantation include the lack of a legal framework for organ donation, clinical expertise, lack of clinical protocols, inadequate laboratory infrastructure especially for HLA testing and crossmatching, and a robust ethical framework.⁶ There is also a requirement for an ethics board to ensure that organ donation is performed without coercion or inducement and is in compliance with the Declaration of Istanbul.⁷

Several centers and groups in high-income countries provide support for the initiation of kidney transplantation in Africa, including Transplant Links, a non-governmental organization based in the United Kingdom.⁸ Similarly, the University of Michigan has an outreach program in Ethiopia.⁹ Ethical transplantation requires a legal framework and ethical committees. Most African countries have an ethical framework for clinical care, but few have specific legislation to cover transplantation.¹⁰

NIGERIA

In Nigeria, kidney transplants first became available in 2000 at St Nicholas hospital in Lagos. Since then, 15

*Dialysis and Transplant Unit, St Nicholas Hospital, Lagos, Nigeria
[†]Department of Nephrology, Gandhi Medical College, Hyderabad, Telangana, India
[‡]Department of Medical Clinics, University of Guadalajara Health Sciences Center, Guadalajara, Jal. Mexico
[§]Department of Medicine and Therapeutics, University of Ghana Medical School. P.O. Box 4236, Accra, Ghana
^{||}Child And Adolescent Health Unit, Faculty of Medicine and Health Sciences, University of Zimbabwe, PO Box A 178, Avondale, Harare, Zimbabwe
[¶]Department of Paediatric Nephrology, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa

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 Address reprint requests to Dwomoa Adu, MD, FRCP, Department of Medicine and Therapeutics, University of Ghana Medical School. P.O. Box 4236, Accra, Ghana. E-mail: Dwoms15@gmail.com
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Table 1. Countries With Transplant Capacity in sub-Saharan Africa, India, and Mexico

Country	Date of First Transplant	Number of Transplant Centers	Number of Transplants Performed Until 2022	Number of Transplants Performed in Past 3 Years
Africa				
South Africa	1966	15	9,011	750
Kenya	July 5, 1978	7	400	160
Mauritius	December 17, 1980	??	389	0
Nigeria	March 6, 2000	16	1,132	546
Cote d'Ivoire	September 24, 2012	3	75	7
Ethiopia	2015	1	137	102
Ghana	2008	1	21	4
Cameroon	November 9, 2021	1	4	4
Mexico	1963	571	55,916	5,873
India	January 1971	550	50,844	27,237

other centers have acquired the capacity to perform kidney transplantation in both public and private health facilities. The more active centers, however, are the private centers, accounting for more than 90% of transplants, and they are located in large urban areas. Public hospitals generally are bedeviled with various problems mitigating against consistency with their clinical programs. These include frequent strikes, interprofessional rivalry and conflicts, poor work ethic, and poor maintenance culture. These also are challenges similar to many other countries in the subregion. Payment for kidney transplantation and other forms of KRT in many of these countries remain out of pocket, with the exceptions being South Africa, Mauritius, and Kenya, where the governments of these countries have actively supported the KRT programs. These countries also have the best-resourced and fastest-growing kidney transplant programs in all of sub-Saharan Africa, and together with Cote d'Ivoire, Nigeria, Angola, and Uganda are the only ones that have enacted human organ transplantation legislation.

The coronavirus disease-2019 (COVID-19) pandemic had a devastating effect on the kidney transplant programs in all units in Nigeria. All units suspended transplantation during the first year of the pandemic, with some resuming in December 2020 when the pandemic numbers decreased. Since then, with better knowledge and experience with managing COVID-19 infections and with the availability of vaccines, the numbers of transplants have increased to pre-COVID levels.

ZIMBABWE

Currently, Zimbabwe does not have a kidney transplant program. However, after initial workup the patient and donor are sent abroad, either to India or South Africa, for their transplant. This is true for many other countries in sub-Saharan Africa. The patients then are followed up after transplantation in Zimbabwe. Very few patients can afford the costs of this life-saving surgery and there is no government subsidy for renal transplantation.

GHANA

In 2008, LD kidney transplantation commenced in Korle Bu Teaching Hospital in Ghana.⁶ The program was supported by a team of transplant surgeons and nephrologists from the University Hospital in Birmingham and by the Transplant Links Community.⁶ Twenty-one transplants were performed between 2008 and 2019, with a 1-year patient and graft survival of 95.2% and 90.5%, respectively, and the 5-year patient and graft survival were 76.2% and 71.4%, respectively.⁶ All the donors are currently in good health. Since then, clinical and surgical expertise was attained locally and through training programs in South Africa and the United Kingdom. The main challenge confronting the sustainability of this program is the lack of a legislative framework to guide organ donation and transplantation. A community survey in Ghana showed that approximately 50% of Ghanaians were willing to donate their kidneys and more than 70% will do so when dead.¹¹ Even though Ghanaians are willing to donate their kidneys, without a legislative framework, it is difficult to establish a DD transplant program. The legislative framework was drafted by the Ghana Attorney General's office with the assistance of the Ghana Kidney Association in 2016 and it currently is awaiting approval by legislators.

Kidney transplantation was suspended temporarily in Ghana after December 2019 because of the COVID-19 pandemic. Seven of our kidney transplant recipient patients developed COVID-19 infection and two of these with severe COVID-19 pneumonia died. The transplant team are planning to resume the transplant program in 2023.

AFRICAN PEDIATRIC TRANSPLANT PERSPECTIVE

Pediatric kidney transplantation is the definitive treatment for infants, children, and adolescents who have end-stage kidney disease.¹² Furthermore, pre-emptive kidney transplantation from a living-related donor before dialysis is superior for children in terms of growth and development as opposed to spending a long time on

dialysis with the associated negative effects, including disruption in school attendance.¹³ Prioritization of children on the transplant waiting list also is important because it allows children to thrive. Unfortunately, in low-resource settings such as Africa, children with kidney disease often come from a long distance from the kidney center, present late, and have very few symptoms apart from poor growth and anemia. This means that the diagnosis of kidney failure is delayed.¹⁴

Congenital abnormalities of the urinary tract often are responsible for infant end-stage kidney disease. However, in many regions, maternal antenatal scans are not performed routinely, resulting in patients presenting late with obstructed renal systems (eg, posterior urethral valves) in need of urologic care. Access to KRT is limited in adults and even more so in children.^{14,15} Efforts by nephrology organizations such as the International Pediatric Nephrology Association, the International Society of Nephrology, the International Society of Peritoneal Dialysis, and the International Pediatric Transplantation Association have supported and expanded training programs of health care professionals.

In addition, access to kidney transplantation is limited for children in low-resource settings, especially for those younger than age 12 years. Such patients often are sent to countries such as India for transplantation at great cost.¹⁶ Rates in Europe for pediatric transplants range from 0 to 13.5 per million children population, compared with very poor rates of less than 4 per million children population in lower-middle-income countries.¹⁷⁻¹⁹ Pediatric kidney transplantation are mostly associated with an adult transplant unit as this gives access to histocompatibility laboratories, radiology, surgeons—both transplant and urology, as well as immunosuppressant drugs. Living donors also need assessment, including careful tissue typing and surgical management for those donating a kidney to pediatric cases. Specific pediatric workup requires input from a multidisciplinary team including pediatricians, pediatric trained nurses, dietitians, and social workers.¹⁹ Before transplantation, it is important to complete a full childhood vaccination protocol, as well as monitoring viral markers post-transplant, such as the Epstein-Barr virus, which is responsible for post-transplant lymphoproliferative disorder. The drugs used for pediatric kidney transplantation are the same as those used for adults, but the metabolism of these may be different in children, making close monitoring of kidney function and drug levels important. Postoperative high dependency care or intensive care facilities for children are needed for careful hemodynamic and fluid monitoring as well as emergency dialysis. There is also a need for post-transplant availability of kidney biopsies in children to assess for rejection, drug toxicity, and viral infections. Adolescent compliance remains a major challenge worldwide and requires a champion for both adults and children together

with psychological support.²⁰ Adult renal and transplant registries are developing in lower-middle-income countries and also are important in pediatric nephrology to assess in future planning of pediatric-specific facilities and governmental advocacy.²¹ The future of KRT and transplantation in low-resource regions seems brighter not only for adults but also for children, with an increase in trained pediatric nephrologists, but a lot of work still is needed.^{22,23} Roadmaps looking at the way forward for kidney disease care for patients of all ages remains important.²⁴

The COVID-19 pandemic impacted the living-related kidney transplant program because the increased need for availability of adult beds in the hospital meant that donors could not be admitted. Pediatric DD transplantation, however, continued during the COVID-19 pandemic.

INDIA

In India, organ transplantation is regulated by the Transplantation of Human Organs Act, 1994, and amended in 2011 to expand the donor pool.²⁵ The act prohibits unethical unrelated transplants, and to increase the donor pool made provisions for deceased organ donations. According to Indian law, explicit consent is required for organ donation. The consent of the next of kin is mandatory after death.²⁷ Presumed donation is not practiced in India. The concept of mandatory brain death declaration has been proposed and practiced legally in some Indian states.

In India, LD kidney transplants are 10 times more frequent than DD transplants.²⁶ Despite being the second-most populous country in the world, India has a low deceased organ donation rate at 0.5 per million population.²⁷ Sociocultural and religious beliefs are the major reasons for low deceased donations in India.²⁸ Organ donation after a cardiac death is rare in India.²⁸ India has approximately 550 transplant centers, and 140 non transplant organ retrieval centers are officially registered with state-appropriate authorities. According to 2020 data, approximately 30,000 patients are on the waiting list for a kidney transplant.²⁶

In 2019, of 9,994 kidney transplants, 11% were from the DD pool and only a meager 2% constituted a pediatric transplantation.²⁶ Gender disparity was predominant, with 28% of kidney recipients being women and 72% men. ABO-incompatible transplantation and paired-kidney-exchange kidney transplantations are performed in a few centers with reasonably good graft and patient survival rates. Financial support is given to patients undergoing organ transplantation in the public sector and this includes the transplant surgery cost and free life-long post-transplant immunosuppression. Most state schemes support kidney transplantation to people living below the poverty line.

In India, rates of death-censored kidney allograft survival at 1, 3, and 5 years after transplant are 94%, 90%,

and 79%, respectively, and the patient survival rates are 92%, 87%, and 83%, respectively. Similar rates of graft and patient survival are reported in elderly patients, with a 5-year survival rate of 82% to 86%.^{29,30}

Barriers for organ transplantation include equity of access, socioeconomic factors, and inadequate health literacy. Similarly, for deceased organ donation, the cultural and religious beliefs, lack of awareness, advocacy among the physician community regarding the declaration process, and misconceptions about utilization are the major factors.³¹⁻³³

Live donor kidney transplantation of foreigners is legal and regulated by the Transplantation of Human Organs Act. Permission for transplantation is obtained from the appropriate authority and clearance from the Embassy is obligatory. No incentives are sanctioned for either live or deceased donation. Organ trafficking and commercialization are prohibited. Directed organ donation or deceased donor chains are not practiced in India.

During the COVID-19 pandemic, India had the second largest number of cases. The first case of COVID-19 infection was reported on January 30, 2020. The COVID-19 pandemic had a significant negative impact on both live and deceased donor kidney transplants in India. There was a sharp decrease in the number of kidney transplants from 9,751 in 2019 to 5,486 in 2020. There was also a reduction in the number of transplants during the second wave of COVID-19 infections in 2021.^{34,35} Consensus guidelines were issued by the Indian Society of Transplant regarding the selection/preparation of recipients and donors.³⁶ With the

availability of vaccination, the rate of renal transplants increased to pre-COVID levels. High mortality rates were observed in renal transplant recipients admitted with COVID infection.³⁶

MEXICO

The first kidney transplant (LD) in Mexico was performed in 1963 followed by a DD kidney transplant in 1966. The lack of infrastructure, trained personnel, high costs, and the absence of legislation regulating organ donation and tissue transplantation resulted in low transplant activity over the following decade. In 1973, regulation on organ and tissue transplantation was introduced for the first time in the Mexican Health Code. In 1984, legislation on organ and tissue donation and transplantation was passed by the Mexican congress, followed by the creation of the National Transplant Registry in 1988.³⁷ In 2000, the transplant registry was replaced by a central coordinating center, the National Transplant Center, and by the establishment of a network of nationwide transplant coordinating centers.^{38,39} In 2003, the Federal Commission for the Protection against Sanitary Risks took over the surveillance and control of transplant activities in the country. Finally, in 2011 and 2013, legislation on organ and tissue retrieval and distribution was passed by congress, delegating this responsibility to the internal transplant committee of each hospital authorized for the practice of transplantation.^{38,40} By law, living organ donation is restricted to adults age 18 years and older, and deceased organ donation requires the

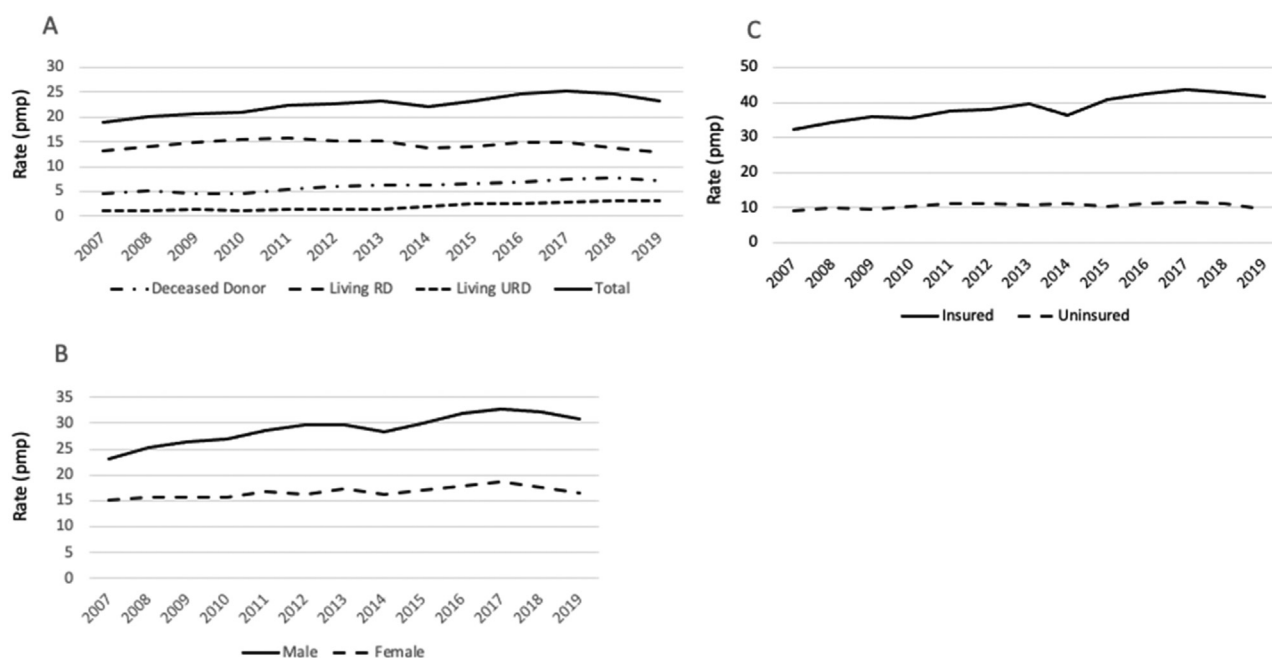


Figure 1. Unadjusted transplant rates per million population (pmp), by (A) donor type, (B) gender, and (C) insurance. RD, related donor; URD, unrelated donor. Reprinted with permission.³⁸

authorization of the next of kin, even if the deceased person had explicitly expressed their wish to donate their organs in case of death. These activities resulted in an increase in kidney transplantation in the country. Between 1984 and 2019, the transplant rate increased from 1.57 to 23.2 per million population (pmp), and the proportion of deceased-organ donor kidney transplantation increased from 12% to 27%.³⁸ By 2019, more than 53,000 kidney transplants had been performed in Mexico.

A recent analysis of more than 34,000 kidney transplants performed between 2007 and 2019 reported that 73% of transplants were from LDs, 27% from DDs, and 9% from living-unrelated donors (LURDs) (Fig. 1A).³⁸ In 2020, the estimated LD graft survival at 1, 2, 3, and 4 years was 95%, 92%, 87%, and 74%, whereas DD graft survival was 88%, 82%, 75%, and 69%, respectively. For recipients of a LD kidney transplant, patient survival at 1, 2, 3, and 4 years was 97%, 96%, 94%, and 87%, whereas for DD recipients patient survival was 90%, 88%, 87%, and 79%, respectively.⁴¹ According to recent data, there are more than 17,000 patients on the national waitlist.

Among the identified barriers to kidney transplantation in Mexico, the most important is the lack of health insurance. Uninsured patients represented only 26% of all transplants and transplantation rates remained significantly lower among the uninsured population (9.3 versus 41.7 pmp) in comparison with patients with health insurance (Fig. 1B)

Similarly, uninsured patients were less likely to be registered on the national transplant waiting list. Only 12% of patients listed in the study period belonged to this population. Uninsured patients must bear the cost of transplant surgery, as well as the cost of maintaining the immunosuppressive therapy.

Similar to reports from other countries,⁴²⁻⁴⁶ gender disparities are prevalent in kidney transplantation in Mexico. Transplant rates were significantly lower in women than in men (30.7 versus 16.4 pmp) (Fig. 1C), and less than 50% of the patients listed in the national transplant list were women. On the contrary, females represented the majority of LD (53.1% versus 46.9%).³⁸ It is known that Mexican women are more likely to be donors, a decision probably driven by economic dependency. In addition, organ donation is identified as another form of nurturing, leading to what has been described as the feminization of organ donation in Mexico.⁴⁷

An additional barrier to transplantation is the bureaucracy of the Mexican public health care system. Successfully navigating the health care system in Mexico requires a combination of favors, personal connections, and political pressure to speed up the work-up for transplantation. Patients who do not have enough economic and intellectual resources to facilitate their access to transplant candidacy seldom receive a transplant.⁴⁵ In

addition, patients without health insurance must often manage a wide range of formal and informal (paperwork) health information.⁴⁸⁻⁵⁰

DD kidney transplantation (7.2 pmp) and deceased organ donation (3.2 pmp) rates are among the lowest in Latin America.⁵¹ The cause of these lower rates is multifactorial. Traditionally, the shortage of deceased organ donors in Mexico has been attributed to public ignorance about organ donation and family refusals to donate. In a recent report, family refusal ranged between 62% and 75%.⁵² However, in a prospective report of potential deceased donors, an overall consent rate of 50% was found, similar to the rate reported in the United States.^{47,53} Furthermore, in two surveys on organ donation in Mexico, 80% of the interviewed persons knew about organ donation, and 75% to 89% would authorize organ donation from a deceased relative.^{54,55} The shortage of deceased organ donors has resulted in an increase of LURDs, especially in private transplant facilities, where LURDs represented 20.2% of all the transplants performed in this setting, in comparison with 6.4% in public facilities, raising concerns of organ commercialization.^{38,56}

Finally, COVID-19 pandemic health policies in Mexico were associated with an important reduction of kidney transplantation, largely in public institutions compared with private facilities (90% versus 42%, respectively). In March 2020, all kidney transplantation activity was suspended, and only life-saving procedures (liver and heart transplants) were allowed. In late June 2020, the program was reactivated using a traffic light system, with increasing levels represented by different colors to regulate public health restrictions. Only transplant facilities with an appropriate number of health care workers, and hospitals with intensive care unit beds, and COVID-19-free zones were allowed to perform transplants.⁵⁷ As a result, kidney transplantation decreased by 89% at public facilities versus by 57% at private. Likewise, an 83% decrease in kidney procurement occurred during the study period. Waiting list additions also were reduced by 82% during the pandemic. Hospital reconversion, a shortage of health care workers low intensive care unit capacity, uncontrolled viral transmission in the community, and the lack of exclusive transplantation and donation centers were identified as the most important factors limiting the number of transplants at public institutions.⁵⁷ Similar to elsewhere, Mexican chronic kidney disease patients have been identified as a high-risk population for COVID-19 infection and mortality.⁵⁸ However, they have never been considered a priority to vaccinate by Mexico's health authorities.

CONCLUSIONS

We describe kidney transplant services in Mexico, India, Ghana, Nigeria, Zimbabwe, and South Africa, the latter

with a focus on children. Access to kidney transplantation is limited in these low- and middle-income countries. In sub-Saharan Africa, only eight countries have kidney transplant programs. Children and women are disproportionately disadvantaged in these programs because of a lack of expertise regarding pediatric care and because women are the predominant donors, not recipients. Most kidney transplants in low- or low-middle-income countries are from live donors, and the lack of legislation often precludes DD, thus further work is needed to enable donation. The COVID pandemic had a deleterious effect on transplant activity, however, the availability of vaccinations and treatments should facilitate transplantation. Transplantation programs in low-resource settings require considerable effort to start and maintain. In the long term, kidney transplantation is the most cost effective and life-sustaining kidney replacement therapy.

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