

# BARRIERS TO EFFECTIVE RENAL CARE IN THE DEVELOPING WORLD

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## BARRIERS TO A FUNCTIONAL RENAL TRANSPLANT PROGRAM IN DEVELOPING COUNTRIES

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A successful kidney transplantation offers the best possible quality of life for patients with end stage renal disease (ESRD). Despite this, renal transplantation rates in the developing world (as with other modalities of renal replacement therapy) are considerably lower than in the developed world.

Identified reasons for this include poverty, low education levels of the populations of these countries, the absence of functional dialysis and transplant units with adequately trained and motivated staff, and the lack of appropriate health policies derived from renal registry data.

Measures to improve the quality of care should center around improvement of the socioeconomic and political scenario in these countries. The peculiarities of renal transplantation in these countries are also discussed. (*Ethn Dis.* 2009;19[Suppl 1]:S1-56-S1-59)

### INTRODUCTION

Kidney transplantation remains the best option in the management of patients with end stage renal disease (ESRD). It confers the best possible quality of life, less morbidity and mortality, and considerable cost savings in the long-term in patients with ESRD.<sup>1</sup> Worldwide, we have seen a steady increase in the prevalence of patients with ESRD, with an estimated annual growth rate of 6%, outstripping the population growth rate of the world of 1.2%.<sup>2</sup> Although the incidence of ESRD appears to be uniform throughout many parts of the world, we find a marked variation among countries in the rates of ESRD patients receiving treatment. Research findings report that the highest rates of ESRD treatment are found in countries of the developed world and the lowest in the developing world.<sup>3</sup>

A comparison of economic strength (expressed as Gross Domestic Product [GDP]) with prevalence of ESRD suggests that economic factors impose restrictions on treatment with further analysis revealing consistently positive relationship until a GDP of \$10,000 per person per year but no correlation thereafter.<sup>2</sup> Accordingly, 60% of all treated ESRD patients are treated in European Union nations, the United States and Japan,<sup>3</sup> with the developed world accounting for more than 90% of transplants worldwide.<sup>4</sup>

The World Bank classification lists countries with GDP <\$9,655(USD) per capita as low and middle income economies and as developing countries.<sup>5</sup> Most of these countries are located in

Africa, Asia, Latin America and the Middle East; and, they generally have unstable governments, inconsistent health priorities and policies, recurrent civil unrest, and rapid population growth. Most often, these nations have total health expenditure (THE) as a percentage of GDP <5%, compared to 10% in the developed world.<sup>5</sup> At the same time, they do not have renal registries to enable accurate estimates of the numbers of patients with ESRD. Instead, estimates are often based on data from dialysis centers, usually based in major cities and leaving most of the rural areas under-served.<sup>6</sup>

Table 1 compares the GDP, THE and dialysis and transplant rates in various selected countries in the developing world with two leading countries in the developed world. In sub-Saharan Africa, consistent renal transplantation is available in only 4 countries namely South Africa, Mauritius, Kenya and Nigeria.

### HISTORICAL ACCOUNT OF KIDNEY TRANSPLANTATION IN NIGERIA

Kidney transplantation first became available in Nigeria at the Saint Nicholas hospital (SNH) in Lagos in March 2000; three other public hospitals have also since commenced kidney transplant programs. Since the year 2000, 99 live donor kidney transplants have been completed, with SNH responsible for 68 of those cases.

Given the population of Nigeria (140 million), an estimate of at least 1,000 new cases of ESRD requiring

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Table 1. GDP per capita and ESRD prevalence and transplant rates

Countries	Nigeria	India	Pakistan	Egypt	Brazil	S Africa	UK	USA
Population (millions)	140	1,103	158	74	186	47	60	298
GDP per capita \$USD	1,400	1,830	2,151	4,274	8,140	8,506	31,308	39,901
THE* as % GDP	5	4.8	2.4	5.8	7.6	8.4	8	15.2
Physicians/1,000	0.28	0.6	0.74	0.54	1.15	0.77	2.3	2.56
ESRD prevalence/million	6	50	55	250	375	75	626	1,110
Transplants/million/year	0.85	3.17	2.5	6.75	17.9	6.3	33	40.2

\* THE = total healthcare expenditure.

transplantation should be expected yearly.<sup>7</sup> The low number of transplants carried out and the equally low numbers (< 1,000 regular patients) on maintenance dialysis programs would suggest that the mortality among these patients would be considerably higher than that observed in the developed world.<sup>7</sup>

The challenge of developing and sustaining these nascent transplant programs is a reflection of similar challenges faced by medical facilities in other parts of the developing world.

Identified impediments to a functional renal transplant program in developing countries include:

- Low literacy and poverty among the general population, with high proportions of the inhabitants of these countries living below the poverty level of 1\$ per day.<sup>8</sup>
- Absence of a renal registry to generate data for policy formulation. Most estimates in the countries of the developing world are based on information derived from the few functional dialysis units and severely underestimate the gravity of the problem.
- Absence of well-formulated health policies and guidelines by the governments of countries in the developing world.
- Lack of basic and essential medical infrastructure in many parts of the developing countries.
- Absence of adequately trained and motivated staff to run the renal replacement programs of these countries.
- Absence of meaningful research in the tertiary health units of these countries.

- Lack of cooperation within and between the various units in these countries.
- Absence of effective national health insurance that includes patients with ESRD.
- Absence of transplant edicts.

The situation is further compounded by poor maintenance dialysis programs, which are essential for any successful transplantation program. Many centers are restricted to urban areas and have few machines, which are often poorly maintained and run by inappropriately trained and unmotivated staff. Many do not have guidelines and protocols for running these units.<sup>7</sup> Many of the trained personnel also emigrate to better paying jobs in the developed world; it is estimated that 20% of Indian nephrologists have emigrated and more Nigerian and Ghanaian nephrologists practice outside their countries than within.<sup>10</sup> Most programs in the developing world are live donor with cadaveric donors forming a negligible part of kidney transplantation.<sup>11</sup>

### Sociocultural factors

In many cultures in the developing world, reverence of the dead is deep rooted and several countries do not permit autopsies. The idea of kidney harvesting for a potential transplant is difficult to comprehend as is the concept of brain death. This is further compounded by the fact that many of these countries do not have cadaveric transplant edicts. India enacted its own edict in 1995, Korea in 2002, Pakistan in 2007 and the Philippines in 2008;

permitting many of these countries to serve as a haven for transplant commercialism and human organ trafficking. Pakistan, India, China, Philippines and South Africa have become noted for transplant tourism with many patients on the waiting lists for cadaver kidneys in many countries of the developed world. Consequently, morbidity and mortality of these patients are often very high.<sup>12</sup>

The donors are often exploited and in India, studies have revealed that 75% of commercial kidney donors remain in debt, 90% reported deterioration in their health and 80% would not recommend donation to others if asked.<sup>13</sup>

### Immunosuppression

Cyclosporine, azathioprine and prednisolone remain the mainstay of immunosuppressive regimes in the developing world. Even though newer drugs reduce the risk of acute rejection and improve long-term graft survival, they are often unaffordable for most patients in the developing world. The use of generic formulations of these medications is common as is the use of diltiazem and ketoconazole to reduce dose requirements of cyclosporine. Antibody use for induction and treatment of rejection is often too expensive, resulting in poorer graft survival rates compared to those from units in the developed world.

Other contributing factors recognized for high post-transplant complication rates in these units include: poor

state of dialysis prior to transplantation; preceding malnutrition; lack of potable water and poor sanitation and sewage disposal; poor crowded living conditions; limited diagnostic facilities to detect preoperative issues affecting transplantation; high prevalence of communicable diseases; and poverty limiting the choice of drugs for prophylaxis and treatment of complications.

### Infections

Infections are, perhaps, the most common post-transplant complication in the developing world. Unlike in the advanced world, where the incidence of infections is low with equally low mortality, in the developing world particularly in the tropics, the incidence and mortality are both much higher.<sup>6</sup> The pattern of infections also differs from that in the developed world. Diarrheal diseases are particularly common due to poor quality potable water and sanitation. Resistance to common antibiotics is not unusual due to indiscriminate abuse of antibiotics (readily available over the counter even without prescriptions) and fake, substandard drugs are common in these countries.

CMV seropositivity is high with 95% of donors and recipients screened at St Nicholas Hospital being positive for CMV 1 gM antibodies. Prophylaxis post-transplant is often with acyclovir as the more potent gancyclovir and valacyclovir are often unavailable and expensive. More sensitive tests such pp65 and PCR for early detection of reactivation are also not available causing treatment to begin late.

Without treatment, higher prevalence of HCV, HBV and consequent chronic liver disease is not uncommon and leads to rapid deterioration of liver function, liver failure and death. Treatment is often unaffordable for patients whose resources have already been depleted by dialysis and transplantation.

Post-transplant tuberculosis is much higher in developing countries averaging

15% as opposed to 0.36% in the developed world.<sup>6</sup> The situation is often compounded by multi-drug resistant strains of the disease and the use of rifampicin for therapy necessitates an increase in the dosage of cyclosporine, already unaffordable for most patients.<sup>14</sup>

As a preventive measure, all patients receiving a transplant at SNH are given oral nystatin for candida for four weeks (or until discharged, whichever is later) and paludrine for malaria, acyclovir for CMV, INH for tuberculosis and septrin for PCP until six months post-transplant. With this treatment regimen, the initial high incidence of CMV infection observed in the early days of the program has regressed with no further mortality from such infections.

### Malignancies

Malignancies are not uncommon in transplant patients in the developing world and, as with infections, they also differ in the incidence and type. Kaposi sarcoma, associated with herpes virus 8, is the most common malignancy encountered, compared to post transplant Lymphoproliferative disease (PTLD) in the developed world. At SNH, of the 68 transplant patients during the last eight years, three have been diagnosed with Kaposi sarcoma, none had PTLD, and one had pancreatic cancer.

### Compliance and monitoring

Compliance and monitoring are often suboptimal as the few transplant units are located in urban areas, restricting adequate followup care for patients who have to travel long distances to attend clinics. The unaffordable cost of medications result in patients taking suboptimal doses of medications and, in some instances, out-dated drugs. Drug-level monitoring is often unavailable and beyond their reach. At SNH, even though the hospital had acquired the technology to do the drug assays, the patients often decline the tests, due to financial constraints.

Diagnosis of rejection is often based on clinical symptoms and signs due to the paucity of the skills to carry out biopsies, the cost of the biopsy, and the absence of adequately trained and experienced histopathologists.

Factors that contribute to poor compliance include poverty, proximity to the hospital, being female and low level of education.<sup>15</sup> Chronic infections and death are more common in the poorly compliant group. In Taiwan, poor compliance was the third cause of graft loss,<sup>16</sup> while at SNH, this was second only to infections.

## SOLUTIONS

The most important solution is to improve the socioeconomic status of the developing world with programs of debt forgiveness, given that many of these countries are spending considerable amounts of their budgets paying interest on loans taken in the past, leaving less for various health programs. These countries must also be encouraged to establish more stable and democratic governments that would focus on improving literacy, sanitation and establishment of functional health programs. The enactment of a solid organ transplant edict by the countries yet to do this is also essential as is the development of renal registries to enable more effective planning. Commencement of national health insurance covering renal replacement therapy is also vital.

Public awareness programs focusing on the causes, prevention and management of kidney disease and emphasizing the safety of live kidney donation must also be encouraged. We need to establish a transparent, independent and functional national kidney foundation to serve the interests of the patients and to act as a unified group presenting their views to government when the need arises. Availability of immunosuppressives at affordable prices, with import duties eliminated and government sub-

sity if possible, should be one of the focuses of such a kidney foundation. Sudan, despite its various political and economic challenges, has been able to achieve such a program and, drugs are available free, allowing patients affordable transplant.

More relevant research must also be carried out by tertiary institutions of the developing countries, with an understanding of the peculiarities of transplantation in the developing world. Further training and motivation in cooperation with centers in the developed world is needed and last, though certainly not least, prevention programs are needed.

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