Disparities in Access to Kidney Transplantation in Developing Countries

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BACKGROUND

Chronic kidney disease (CKD) is a global health problem with nearly 0.1% of the world's population suffering from end-stage kidney disease (ESKD).[1] The availability and accessibility to treatments for ESKD differ around the globe because of variations in healthcare budgets and availability of treatments. Although the prevalence of ESKD in low-income countries (LICs, 0.05%) and lower middle–income countries (L-MICs, 0.07%) is estimated to be lower than in high-income countries (HICs, 0.2%), or potentially underdiagnosed, the proportion of patients who are not receiving effective treatment is much higher in LICs (96%) and L-MICs (90%) compared with upper middle–income countries (U-MICs, 70%) and HICs (40%).[2] In some L-MICs, it is impossible to support hemodialysis treatment for every ESKD patient, and most patients are unable to pay for dialysis out of pocket.[2]

Access to kidney replacement therapy (KRT) and distribution of KRT is thus highly inequitable. In a recent report investigating international disparities for ESKD treatment, >90% of U-MICs and HICs reported having kidney transplant services, with >85% of these countries offering both living and deceased donor transplants; LICs had the lowest availability of kidney transplant services (12%), with living donor transplants as the only organ source.[3] Moreover, the successful implementation of kidney transplant programs in LICs and L-MICs is hampered by many challenges. Thus, understanding the access to transplantation in these countries, in addition to specific challenges, appears paramount.

The aim of this work led by fellows of the International Society of Nephrology (ISN) and country representatives from 23 LICs, L-MICs, and U-MICs delineates international disparities in delivering proper kidney transplantation service for patients with ESKD and proposes a roadmap toward equitable access to kidney transplantation globally.

GENERAL INFORMATION OF LOW- AND MIDDLE-INCOME COUNTRIES

Demographic and economic country profiles were referenced from the World Bank[4] and World Health Organization[5] online data source, stratified by World Bank ranking of country's economies, and presented in Table 1. Information on national transplant programs was collected from each ISN fellow or country representative and literature search (Table 2).

Among the surveyed 4 LICs, Nepal and Tajikistan have relatively higher gross national income per capita (compared with Afghanistan and the Democratic Republic of Congo, DRC), and their governments partially support the cost of kidney transplantation. There is no national transplant program in DRC; transplant costs are not covered in Afghanistan. Only Tajikistan reports on a partial transplant registry and national transplant coordination with some costs for transplantation covered.

Among the surveyed 14 L-MICs, only Cameroon has not started a regular kidney transplant program. Although Moldova, Algeria, and Palestine cover all costs for transplantation, Ghana and Cameroon provide no coverage, and the remaining 9 L-MICs provide only partial coverage. A nationwide allocation and procurement service has been launched in Bolivia, Egypt, India, Moldova, Morocco, and Uzbekistan; however, a transplant registry has not been implemented yet in Cameroon, Egypt, Ghana, Morocco, and Pakistan.

Transplant programs in LICs, L-MICs, and even U-MICs suffer a number of challenges that adversely impact effectiveness, solidarity, development, and the ability to control unethical practices (Table 2).

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TABLE 1.
Country profiles

Country (by world bank rank)	Population (2019), million	Population density person/ km^2 (2018)	Gross national income per capita (PPP Intl $, 2019) Atlas Method	Current health expenditure per capita (PPP Intl $, 2017)	Current health expenditure as % of GDP (2017)	Life expectancy at birth total (y, 2018)
Low-income countries						
Afghanistan	38.04	56.9	540	174.7	11.8	64
DRC	86.7	37.1	520	37.3	3.98	60
Nepal	28.60	195.9	1090	150.1	5.55	70
Tajikistan	9.32	65.6	1030	231.4	7.23	71
Lower-middle-income countries						
Bolivia	11.51	10.5	3530	491.6	6.44	71
Cameroon	25.87	53.3	1500	173.8	4.67	59
Egypt	100.388	98.9	2690	613.8	5.29	72
Ghana	30.41	130.8	2220	146.8	3.26	64
India	1.366	454.9	2130	253.3	3.53	69
Kenya	52.57	90.3	1750	158.2	4.80	66
Kyrgyzstan	6.4	32.9	1240	241.2	6.19	71
Moldova	2.65	123.5	3930	476.7	7.01	72
Morocco	36.47	80.7	3190	438.1	5.25	76
Pakistan	216.5	275.3	1530	160.5	2.90	67
Palestine[a]	4.68	759.0	3710	330.3	9.3	74
Ukraine	44.38	77.0	3370	584.6	7.00	72
Uzbekistan	33.5	77.5	1800	447.8	6.41	72
Algeria	43	17.7	3970	974.8	6.37	77
Upper-middle-income countries						
Armenia	2.95	103.7	4680	1001	10.36	75
Kazakhstan	18.5	6.8	8810	820.3	3.13	73
Malaysia	31.9	96.0	11 200	1139	3.86	76
Perú	32.5	25.0	6740	681.2	5.00	77
Turkey	83.4	107.0	9610	1180	4.22	77

[a]Data on health expenditure were obtained from Palestinian Central Bureau of Statistics website: http://www.pcbs.gov.ps/PCBS_2012/Publications.aspx?CatId=56.
DRC, Democratic Republic of Congo; GDP, gross domestic product; Intl $, international dollar; PPP, purchasing power parity.

All 5 U-MICs, Armenia, Kazakhstan, Malaysia, Peru, and Turkey, have established kidney transplant programs with at least partial coverage of transplant expenses, national transplant coordination, and partial or full transplantation registries.

CULTURAL, RELIGIOUS, AND EDUCATIONAL BARRIERS

Country-specific cultural characteristics shape the acceptance of organ donation, the concept of brain death, and the overall perspective on treating patients with ESKD including transplantation. The majority of countries (15 of 23) reported on cultural and spiritual factors as barriers to organ transplantation. Some ethnic minorities have been identified as having misconceptions about organ transplantation due to lack of education, religious myths, medical distrust, or fear of premature death of donors; racism appears as a driving force by some, leading to reluctance in organ donation. Patients with ESKD do not feel comfortable in asking family members to donate, fearing complications, having concerns about burdening the family, and being concerned about the impact that donation may have on family relations.

Religious beliefs play a significant role in patients' views and attitudes toward transplantation.[6] Islam, for example, emphasizes the importance of saving the lives of others but forbids the violation of the human body, whether alive or dead. Different associations of Islamic law have put forward regulations for organ donation, either living or deceased, considering the fine balance between saving lives while avoiding potential harm to the donor. However, in LICs and L-MICs, regulations concerned with deceased donation have not convinced the entire Muslim population, mainly because of cultural, environmental, and misinterpreted religious reasons. Consequently, deceased donation is scarce in most low-income and lower middle–income Islamic countries that have therefore expanded living donation with risks for unethical practices.

In general, Christianity is supportive of organ transplantation and donation. The Catholic, Anglican, and Protestant churches agree that organ donation is an act of selflessness, exemplifying Christian love. The Church of Jesus Christ of the Latter-day Saints teaches that organ donation should be left to an individual decision. Jehovah's Witnesses do not accept blood transfusion and will leave organ transplantation to the individual's discretion. However, some still have concerns about living donations, questioning the passage of the donor's blood through their organ.

Recognition and acceptance of "brain death" are a prerequisite to establishing deceased donor transplant programs. However, this is a quite challenging issue in most LICs and MICs. Thirteen of 23 countries reported misconceptions of brain death by patients' relatives. This lack

TABLE 2.

Kidney transplant services and barriers in middle- and low-income countries

Country	Transplant Registry	Health coverage	Transplant national coordination	Regular transplant program started	Donor type available	Follow-up team	Barriers category[a]	Ethical laws	Immigrant transplant policy	Organ trafficking
Low-income countries										
Afghanistan	No	No coverage	No	2015	LIV	OTHER	C, F, G, H	No	No	Yes
DRC	No	No coverage	No	Not started yet	No	NEPH/OTHER	F, G	No	No	Possible
Nepal	No	Partial coverage	No	2008	LIV and DEC	NEPH	A, C, D, G	Yes	Yes	Yes
Tajikistan	Partially	Partial coverage	Yes	2010	LIV	NEPH	C, D	Yes	Yes	No
Lower-middle–income countries										
Bolivia	Partially	Partial coverage	Yes	2014	LIV and DEC	NEPH	A, C, D, E, G, H	Yes	Yes	No
Cameroon	No	No coverage	No	Not started yet	No	No	F, G, H	No	No	No
Egypt	No	Partial coverage	Yes	1976	LIV	NEPH	A, C, D, E	Yes	Yes	Possible
Ghana	No	No coverage	No	2008	LIV	NEPH	C, F, G, H	In process	No	Possible
India	Partially	Partial coverage	Yes	1971	LIV and DEC	NEPH/SUR	A, D, G	Yes	Yes	Yes
Kenya	Yes	Partial coverage	No	2006	LIV and DEC	NEPH	A, C, G	Yes	No	No
Kyrgyzstan	Partially	Partial coverage	No	2018	LIV	NEPH	A, C, D,F, H	In process	No	No
Moldova	Yes	Full coverage	Yes	2012	LIV and DEC	NEPH/URO	B, C, D	Yes	No	No
Morocco	No	Partial coverage	Yes	1985	LIV and DEC	NEPH	A, B, C, D	Yes	No	No
Pakistan	No	Partial coverage	No	1979	LIV	NEPH	C, F, G,	Yes	Yes	Yes
Palestine	Partially	Full coverage	No	2010	LIV	NEPH	A	Yes	No	No
Ukraine	Partially	Partial coverage	No	2006	LIV and DEC	NEPH/OTH	A, C, D	In process	No	No
Uzbekistan	Partially	Partial coverage	Yes	2017	LIV	NEPH	A, C, D	In process	No	No
Algeria	Yes	Full coverage	Yes	1986	LIV and DEC	NEPH	A, B, D	Yes	Yes	No
Upper-middle–income countries										
Armenia	Yes	Partial coverage	Yes	2002	LIV	NEPH	C	Yes	No	No
Kazakhstan	Partially	Full coverage	Yes	2012	LIV and DEC	NEPH	A, C, D	Yes	No	No
Malaysia	Yes	Partial coverage	Yes	1975	LIV and DEC	NEPH	A, B, C, G, H	Yes	No	Possible
Peru	Partially	Full coverage	Yes	1969	LIV and DEC	NEPH	A, C, D, H	Yes	No	No
Turkey	Yes	Full coverage	Yes	1968	LIV and DEC	NEPH	A, C, D	Yes	Yes	No

[a]Barriers category: A, cultural/spiritual impediments; B, low number of referrals; C, donor shortage; D, long waiting time; E, organ trafficking; F, lack of legal framework; G, insufficient financial support; H, lack of tissue typing.

DEC, deceased; DRC, Democratic Republic of Congo; LIV, live; NEPH, nephrologists; OTH, other specialities; SUR, surgery; URO, urologists.

of understanding represents a major barrier to deceased transplantation.

Many patients present with advanced CKD leading to increased mortality even before considering kidney transplantation. In addition, poverty and the unequal distribution of hemodialysis machines in some countries add to high mortality rates.[7] In our report, 4 countries (Algeria, Malaysia, Moldova, and Morocco) reported low referral rates as a barrier to transplantation.

Limited expertise with few nephrologists represents another challenge. The median number of nephrologists worldwide is 9.95 per million population (pmp); the "density" of nephrologists increases from 0.2 pmp in LICs to 1.6 pmp in L-MICs, 10.8 pmp in U-MICs, and 23.2 pmp in HICs.[1] In 1 study, only 43% of nephrologists dedicated some time to educate patients about transplantation within the first 3 mo of dialysis treatment.[8] Consequently, many patients are not well informed about transplantation as a modality for KRT, and there may even be a financial incentive to keep patients on dialysis in some countries.

ORGAN SHORTAGE AND PROLONGED WAITING TIME

The discrepancy between demand and supply is even more obvious in LICs and L-MICs. The lack of a deceased donor program in 11 of 23 countries we surveyed aggravates organ shortage furthermore. Although Nepal is the only LIC with both living and deceased donation programs, Armenia is the only U-MIC without a deceased donor program. Globally, transplant rates of living donor kidney average 5.3 pmp, ranging from 0.4 pmp in Myanmar to 33.2 pmp in Turkey. Among the 75 countries that offer deceased kidney transplants worldwide, the average volume is 15.1 pmp,[8] and rates increase with income level. Overall, deceased donor kidney transplant rates are below the global average in Africa, Latin America, the Middle East, North and East Asia, Newly Independent States, and Russia.[9]

Organ shortage will result in an unduly long waiting list. At Mansoura Urology and Nephrology Center in Egypt, where only living-related transplants are performed, waittimes for a matched donor and recipient average approximately 1.5 y.

TRANSPLANT TOURISM, ORGAN TRAFFICKING, AND LEGAL CHALLENGERS

The Declaration of Istanbul (DoI) and the Declaration of Istanbul Custodian Group defined and continue to battle transplant tourism and organ trafficking (OT).[10] According to the World Health Organization's Second

Consultation on Human Transplantation in 2007, OT accounts for 5%–10% of the kidney transplants annually.[9]

In our report, possible OT was present in 8 countries and more prominent in LICs (3 of 4) than in L-MICs (4 of 14) and U-MICs (1 of 5). This is because tourism trafficking and OT are linked to a lack of national transplant programs, organ shortage, absence of deceased donation, lack of specific regulations for immigrants in need of kidney transplantation, and religious and cultural beliefs that are not in support of donation. Unfortunately, it is particularly the vulnerable and poor population that is suffering and exploited by organ brokers to sell their organs.

A legal framework is mandatory and should comply with the principles of DoI,[10] aiming to ensure donor and recipient safety and equity in access to transplantation. Moreover, brain death needs to be defined, and the rules governing deceased donation, allocation, and recipient listing need to be clear. Seven countries (2 LICs and 5 L-MICs) are still lacking legal frameworks for deceased donation and do not regulate transplant activities involving immigrants. Except for Afghanistan, all countries have ongoing attempts to implement legal frameworks, and all countries with transplant programs are expected to adopt the principles of DoI. We assume that professional societies base their work on the principles of DoI. Individuals violating those principles should therefore not be members of those societies. Moreover, pharmaceutical companies and public and private funding agencies must affirm that any clinical trial or support is not in violation of DoI.

FINANCIAL AND ORGANIZATIONAL BARRIERS

Globally, 64% of all countries provide full coverage for kidney transplantation, with 43% charging fees at the point of delivery.[1] LICs have the highest private funding for kidney transplantation with the least governmental support. Those countries also suffer shortages especially in their workforce (90%), particularly for transplant coordinators.[9] All LICs in our survey reported insufficient financial support with the exception of Tajikistan. Malaysia was the only U-MIC to report insufficient financial support. Three of 5 U-MICs provide full financial coverage for kidney transplantation, whereas Moldova, Palestine, and Algeria (3 of 14) were the only L-MICs to provide full coverage.

Seven countries reported having insufficient tissue typing services. In most LICs and L-MICs, tissue typing facilities are central, challenging the successful implementation of deceased-donation programs. Moreover, financial constraints also limit best practice guidelines. In some transplant facilities, for example, anti-HLA antibodies are not routinely screened pretransplant. In Malaysia, for example, HLA-typing can only be offered infrequently as reagents are often not available.

Renal registries are essential for monitoring trends and outcomes as a basis for policymaking. Globally, there are many renal registries (144 in 2014), yet only a small minority have comprehensive, readily accessible patient-level data, and these tend to be in HICs (17 in 2014). In much of the Asia-Pacific region, the Middle East, and Africa, registries were either absent or had limited data or poor accessibility. Six of 23 surveyed countries reported having transplant registries. Armenia, Moldova, and Algeria are the only LICs and L-MICs with established transplant registries; Palestine, Tajikistan, and Ukraine have ongoing efforts to establish transplant registries. Among the 6 African countries in our survey, only Algeria and Kenya have transplant registry. Only about half of the surveyed countries provide national transplant coordination (LICs: 1 of 4; L-MICs: 7 of 14; U-MICs: 5 of 5).

A ROADMAP FORWARD

Developing countries face multiple challenges to provide universal and equitable access to kidney transplantation. Although there are commonalities, each country needs to identify its own needs to set up a successful transplant program.

Overall, educational and governmental awareness programs should be encouraged to increase public acceptance of both live and deceased donation and to correct faulty beliefs preventing deceased donation. It is also necessary to convince both policymakers and the public to implement comprehensive kidney transplant programs. In many countries, the concept of brain death needs to be clarified and legislations for deceased donation need to be adopted to pave the way for a deceased transplant program.

Another effective way to expand the donor pool and thus to shorten waiting times is to encourage paired or pooled kidney donation programs in countries with regular transplant activities. Strict regulations stopping OT are also much needed. The fight against OT should have special governmental concerns with extensive inspection measures and tough penalties.

Improvement in healthcare funding to reimburse transplant cost is mandatory to establish national transplant programs. Deficient infrastructural domains in every country need to be identified and addressed in collaboration with transplant-oriented professional bodies and well-established transplant programs. Examples of such collaborations include the sister center projects between developing and developed transplant centers and the fellowship training opportunities for nephrologists from developing countries to lead their transplant programs.

CONCLUSION

LICs and L-MICs suffer major challenges to develop transplant programs and to provide equitable access to kidney transplantation. Large-scale, well-planned solutions to these obstacles include accessible public health and mandate international efforts to improve the care of patients with ESKD.

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