

How To Promote Transplantation In Pakistan And Establish Quality Centers

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IMPORTANCE Chronic kidney disease is a rapidly growing health care concern in Pakistan with limited capacity to be addressed due to poorly organized medical services. According to United Nations Population and World Bank, the Pakistan population is more than 220 million. Transplant program development will require extensive commitment and sacrifice. The biggest challenge will be to start performing deceased donor transplants and standardizing the existing living donor transplantation programs to improve outcomes. It is a daunting task but can be achieved with proper leadership and responsibility. There will be hurdles, setbacks, and delays, but these can be overcome with perseverance, focus and hard work. Those who have been granted the opportunity to train at the highest levels abroad can participate and provide support in this noble cause.

KEYWORDS Transplant Centers; Quality Assurance; Transplant Centers; Logistics; Quality Protocols

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Invited Commentary

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Chronic kidney disease is a rapidly growing health care concern in Pakistan with limited capacity to be addressed due to poorly organized medical services.

According to United Nations Population and World Bank, the Pakistan population is more than 220 million^{1,2}. The top three reasons for chronic kidney disease in Pakistan are diabetes mellitus, hypertension, and glomerulonephritis^{3,4}. Patient diagnosed with chronic renal failure is increasing with an estimated annual incidence of > 100 cases of end stage renal disease (ESRD) per million population⁵. The average age of patients diagnosed ESRD are in their 40s⁶. Due to lack of national policies and systematic databases, most information comes from individual centers. Experts in the health care industry believe that the prevalence of chronic kidney disease and end stage renal disease is much higher than the available statistics⁵.

A potential cause for the increasing incidence of ESRD is because chronic medical conditions are often not diagnosed in a timely manner or optimally managed. This leads to the need for ESRD treatment with dialysis much earlier compared to countries with greater resources⁶. When patients progress to dialysis the patient and family are left with difficult decisions. Most patients who start dialysis die because they stop treatments due to cost within the first three months or lack of available dialysis services close to home. Due to cost and lack of access, many families are told the only treatment choice is kidney transplant.

There is consensus the government and private sector need to work together to develop preventive programs for chronic diseases such as diabetes mellitus and hypertension and increase public awareness⁶. Another urgent question is how to help patients who have already developed end stage renal disease and are left to decide between dialysis versus transplantation. Kidney transplant is proven to improve quality and longevity of life compared to dialysis. However, most of this data comes from developed societies such as United States, Europe, and Japan⁷.

The world is becoming a global village, and medical tourism has increased in the past several decades. Historically, wealthy people from Pakistan have travelled to England and United States for medical needs. This practice led to fundamental problems in our health system, as the privileged class were able to access care elsewhere and efforts were not implemented to develop the hospitals and institutions in Pakistan. In recent years, desperate families outside the privileged class have travelled to other countries and fallen victim to opportunist organizations with false advertising. By 2030, the number of patients receiving dialysis around the world is projected to increase to 5.4 million and most of this increase will be in the developing countries of Asia and Africa⁸.

The Sindh Institute of Urology and Transplantation (SIUT) in Pakistan has been making efforts to overcome health disparities. They have done a phenomenal job in providing

complex care to people irrespective of their religious beliefs, ethnicity, and socio-economic status. However, access remains limited⁹. SIUT performs more than 1100 dialysis sessions per day and has performed more than 6000 transplants since 1980's, but alone they cannot keep up with need in Pakistan⁹. Other hospitals have started transplant programs in different parts of country due to increasing incidence of end stage renal disease. It has become evident with every passing day that an organized, sustainable, and financially sound transplant-specific hospital system is needed to provide the highest level of care to this underserved population in Pakistan.

There are certain questions that need to be answered before we take on this highly complex issue. We will also need to work on different issues simultaneously to achieve the target faster as we are trying to catch up right now.

SECTION I:

We will initially focus on how to promote transplantation followed by team building and how lessons learned during COVID-19 can help achieve those goals.

1. Ethics
2. Religious beliefs
3. Community beliefs
4. Pharmaceutical Support
5. Transplant Team
6. Regulatory compliance
7. Government Support
8. Access to transplant
9. Role of telemedicine
10. Importance of post-transplant care

Ethical Concerns: Transplant ethics deals with issues related both to the transplantation process and organ allocation. Access to transplant specifically for under privileged population and fair allocation of deceased donor organs are of utmost importance. The declaration of Istanbul strongly condemns organ trafficking, transplant tourism, and commercialism¹⁰. Pakistan passed a law "Transplantation of Human Organs and Tissue Ordinance 2007" to curb illegal transplant activity^{11,12}. Also, there are separate issues related to living and deceased organ donation.

In living donation, the first rule is to protect the donor at all costs. There should be no coercion in living donation, unfortunately, family members are often pressured to donate in Pakistan. Living donation should also be based on compassion without financial gains. Paid donation and organ trading has scarred the field of transplantation especially in Indian sub-continent and middle east. The transplant center and physician have the utmost responsibility to protect living donors from family

retribution if they elect not to donate. Living donor well-being is also extremely important, and donors should be able to resume their normal life, including work and other responsibilities, after donation. Special caution should be considered when assessing younger donors, specifically women. Every effort should be made to assess the donor's risk to develop potential complications in the future. If the work up reveals any potential risk, that risk should be clearly communicated to the donor first and then the rest of the family and recipient at the discretion of the donor. Donors should be highly encouraged to follow up with his or her chronic health care maintenance and practice preventive health measures to avoid the need for dialysis themselves in the future

Although deceased donation is non-existent in Pakistan, it could offer a lifesaving option for recipients who have no living donor available and to meet the anticipated increased demand for transplant in the future. However, it does raise its own ethical questions for both the donor and allocation to recipients.

Donor issues include controversies such as the definition of brain versus cardiac death, responsibility for the costs of laboratory and imaging tests, and how to obtain consent and an adequate past medical history from the family prior to donation. The family should always maintain the right to withdraw consent without any explanation. A systematic system must be in place for persons to register as an organ donor so their wishes can be known and respected after death. Dr. Schroff in his editorial comment talked about the challenges in setting up a deceased organ donation in South Asia and projected demand¹³.

Organ allocation of deceased donor organs should be equitable, regardless of social, religious, or economic status. This process will only be successful if everyone believes it is fair and all recipients are treated equally. The development of governing bodies independent of government influence will be highly recommended to provide oversight of transplant programs.

Religious Beliefs: Religious beliefs are of the utmost importance and should be very carefully considered in Pakistan. Incorporating religious beliefs when providing transplantation support and promoting organ donation is crucial. There are numerous Islamic teachings discussing the rewards for saving humanity, yet cultural barriers often prohibit donation. In general, the Muslim community is viewed as being opposed to organ donation. However, it is the opinion of the author that this view is related to inadequate education and access to transplant to members of this religious group. Consistency among different sects in the Islamic world on this topic would be beneficial for promoting organ donation. Scholars from different sects should be invited to comment and open discussions should be encouraged to create harmony in the public opinion.

In addition to patient education, the views of different faiths should be incorporated into the donation process. Respect of the human body after death is practiced in all religions but minimizing trauma to the human body and early burial are particularly emphasized in the Islamic faith. The deceased donation process should guarantee adherence to these practices. Deceased donation from female donors can or will be a challenge in the beginning but with good practices in place and a dedicated team all those hurdles can be overcome. People from all faiths should be treated at the same level and their rights should be protected at all costs. There should be no discrimination based on religion in organ donation.

Community beliefs: The local community structures and cultural practices in Pakistan can be vastly different among provinces. Local traditions can be as influential as religious beliefs. Community leaders and other stakeholders need to be educated regarding organ transplantation to promote organ donation in their respective areas. Community campaigns led by local community leaders and health care workers can address misbeliefs and fears related to transplant.

Pharmaceutical Support: Successful organ transplant requires lifelong immunosuppression, thus pharmaceutical support and access to medications is of the utmost importance. As evident from literature, one of the most common causes for graft failure is non-compliance with medications secondary to financial reasons. Coverage of end stage renal disease and post-transplant care under the health insurance system in Pakistan needs to be addressed. Patients are mostly responsible to pay for all costs out of pocket, which is not feasible for most patients. It is important to assure availability of induction and maintenance of immunosuppression at an affordable price. Support from government subsidies and pharmaceutical companies will be needed initially until a sustainable process is designed and implemented. SIUT is an example of an institution that has done an extraordinary job of providing immunosuppression free of cost in a sustainable manner based on philanthropic donations^{14,15}. However, higher volumes in the future may require other funding sources. Another consideration is ensuring medications are obtained from reliable sources due to historical issues with counterfeit medications in Pakistan. The new Health card being introduced by the government should cover the cost of immunosuppressants. If charity funding is available, it can be utilized to help cover medication costs.

Transplant team: The transplant team is a multi-disciplinary team working together to optimize care over the course of time. Performing the transplant surgery is not solely the goal but rather maintaining the function of the graft over a long period of time is the marker of success. A

successful kidney transplant team should include, but is not limited to these individuals:

- Surgeon
- Nephrologist
- Physician extenders, such as nurse practitioner or physician assistant
- ICU support staff
- Dialysis support staff
- Pharmacist
- Histocompatibility lab
- Radiologist
- Interventional radiologist
- Pathologist
- Transplant coordinators
- Social worker
- Nursing staff
- Dietitian
- Quality assurance staff
- Organ recovery team / donor management team

The transplant journey includes pre-transplant preparation, organ recovery, transplant surgery, post-operative care and long term follow up. Different organs such as kidney, liver, heart, and lung may have nuanced processes, but generally follow the same principles. Everyone on the team has a specific role, and they all come together to complete the picture. Team development will be discussed in the next section.

Regulatory Compliance: Regulatory compliance is vital to maintaining quality programs. Every effort should be made to standardize the process across the nation with some center-specific preferences allowed. A centralized regulatory body should be completely out of government influence and its board of directors should be held to the highest moral standards. Transplant programs should be audited on a scheduled basis and make every effort to stay in compliance. Centers should be given the opportunity to correct deficiencies that are identified, but persistent non-compliance should lead to prohibition of the program.

The regulatory body should also establish connections with the international transplant community with an intent to adapt practices in line with international standards.

Government Support: Robust legislation at national and provincial levels is required to setup a national transplantation program. Rizvi et al. published articles regarding successful government public sector cooperation and advancing transplantation^{14,15}. Policy making at a national level with laws to protect living donors, recipients and transplant healthcare providers are necessary. In addition to living transplant, government support will be required to pave the path for deceased donation. A national database with help of NADRA (National Database and Registration Authority) like UNOS (United Network for Organ Sharing) in US can be introduced. Preventive measures implemented by the government to minimize the burden of chronic diseases on society will also help

facilitate transplantation, as there will be less mismatch in supply and demand. Collaboration with the World Health Organization (WHO) can help establish short- and long-term plans for chronic conditions. Additionally, American Society of Transplantation, American Society of Transplant Surgeons (ASTS), European and other societies have programs to facilitate and promote transplantation in underdeveloped countries.

Standardized data collection is another area requiring governmental assistance to establish quality programs. Accurate data collection, analysis and policy making based on this data are foundational steps regarding any project's success.

Pakistan spends less than one percent of its growth domestic product (GDP) on the health sector. A growing population and an increasing incidence of chronic diseases such as diabetes mellitus, hypertension, ischemic heart disease, chronic kidney disease and obesity will be a great challenge in the coming decades. Our health system is not equipped to take care of these patients and the government should encourage the private sector to invest in the health industry with appropriate laws and oversight.

Access to Transplantation: Access to transplantation is a large obstacle in developing countries. Researchers in United States have developed an Access to Transplantation Score which assesses health care disparities and chances to get a kidney transplant¹⁶. Factors that play a significant role in access to transplantation are individual and community related. Individual factors will include blood type, disease diagnosis, age of the patient, gender (women have already decreased access to health care), patient education status, and socio-economic status. Community factors include, but are not limited to, public sector education, health care professional education, internet access and transportation. Tools must be developed to reach those with decreased access to transplant. Web portals may facilitate access to materials related to transplantation to improve understanding for the general population. In the past, philanthropic efforts have proven to be successful in providing these types of services. Community awareness programs like public seminars, health care professionals' workshops, community awareness walks, free camps and social media advertisements could be introduced.

Role of Telemedicine: One of the major changes in healthcare during the COVID-19 pandemic is role of telemedicine. Many new telemedicine systems have been developed in a very short period, which has significantly opened new horizons in patient care and how patients with chronic diseases are managed. Internet access and bandwidth can be limiting factors in certain settings. Underdeveloped countries can pursue strategies to implement telemedicine and help their population achieve better health and address health care disparities.

Government and private sectors should collaborate to achieve this goal. Telemedicine can be used to perform pre-transplant evaluations and provide long term care when the patient is stable. This concept can be heavily utilized in management of other chronic disease states as well, such as diabetes mellitus, hypertension, chronic kidney disease and obesity.

Telemedicine platforms can also be used for patient education, health care professional training and conference attendance at regional, national, and international levels. This can allow collaboration among transplant professionals on difficult case managements.

Post-Transplant Care: Post-transplant care is one of the most important pillars to avoid complications and increase the longevity of the graft. Lifelong follow up should be provided to transplant patients¹⁷. Surgical success is meaningless if the patient is not compliant with post-transplant follow up. A well-trained transplant nephrologist needs to take the responsibility of long term follow up after a successful surgery. Due to the shortage of a reliable primary care system, the management of diabetes mellitus, hypertension, and hyperlipidemia will likely be the responsibility of the transplant team. Collaboration with specialized consultants can be obtained based on the complexity of issues.

Non-compliance with medications secondary to socio-economic reasons is a tragedy and should be avoided at every cost. Patients should be thoroughly educated regarding medication compliance with both transplant medications and other chronic disease state medications, as those disease processes will affect the new kidney if not properly controlled. If a patient has remained stable for a long period a decision regarding referral back to local nephrologist is purely on the managing team.

Early intervention to detect and prevent rejection helps improve long term graft survival. Acute rejection in the first year after transplant has a direct correlation with graft longevity, and late rejections are often difficult to treat. A high index of suspicion and development of a center-specific case discussion session can be helpful to identify and manage those issues.

The role of the multi-disciplinary team in pre- and long-term care cannot be over emphasized. Multiple providers discussing solutions to complex issues after initial work up can save valuable time and resources.

SECTION II

We will discuss the logistics of developing a transplant team and program.

Development of a transplant team and program is a time consuming and methodical process requiring patience, persistence, talent recruitment and financial resources. There have been success stories of transplant programs being established with limited resources in the Indian sub-continent. Every single person on the list mentioned are required to manage different aspects of the transplant course. Transplant team expertise depends on organ type, for example liver transplant team will require different expertise than a kidney transplant team. For example, a dedicated anesthesia team is necessary for liver transplant programs.

Competent surgeons, operating room technicians and nursing staff are extremely important for the transplant procedure. A surgeon's training, skill and experience are valuable assets. Minimizing re-operation and surgical complications play a significant role in this immunocompromised patient population. Close follow up in the early post-operative period by the surgical team is also beneficial. There are surgeons of Pakistani descent who have been trained in world's best institutions in the United States and England who can be approached and incentivized to establish transplant programs in Pakistan. To develop a sustainable work force, international-level fellowship training institutions must be developed in Pakistan. ASTS has developed a robust fellowship training program in the United States and aids international partners in other countries. Such collaboration can open elective opportunities or additional training options abroad with the intent to return to Pakistan for service. Aligning training standards, educational materials and curriculum will provide easier systems integration, which is important for a long-term partnership. Teleconferencing can provide options for training, collaboration, and attendance of conferences, particularly during the COVID-19 pandemic and with financial constraints. A market analysis for work force supply and demand should be carefully considered because an inability to find a desirable job will lead to demotivation and lack of interest for future candidates.

The same concepts apply to other members of the transplant team where advanced training is available, such as nephrologist, pathologist, histocompatibility laboratory staff, pharmacist, etc. A transplant nephrologist with dedicated fellowship in transplant or having good transplant exposure in nephrology fellowship is a key team member to help improve pre- and post-transplant outcomes. There are no dedicated transplant fellowships for intensive care, radiology, or interventional radiology, but some physicians have developed advanced skills in taking care of these complex patients. There are dedicated fellowship training programs for transplant pathologists. Other physicians who also play a significant role in program development are cardiologist and pulmonologist with special interest in end stage renal disease patients to provide a thorough cardiac/pulmonary assessment with a

low threshold for invasive intervention. Transplant infectious disease consultant is a luxury to have. Transplant pharmacists are a quintessential team member, and no transplant is complete without one. After completion of pharmacy training, additional training is encouraged to work as an independent full-time transplant pharmacist.

Transplant nurse coordinators have multiple roles, which include but not limited to pre-transplant work up completion, ensuring regulatory compliance, and post-transplant patient care. Development of dedicated hospital floor nurses is ideal to take care of transplant recipients post-operatively, given the unique needs of these patients. Special dedication and motivation are required to go through the learning process for these providers.

Social workers are essential to assess patients' home conditions, social support, transportation options, coping skills, ability to manage transplant regimens, and advocating for the support they might, among other factors. They can help with patients struggling to afford their medications or dealing with other major life events that could impact compliance.

Dieticians are important to optimize patients' dietary management in the pre- and post-transplant setting. They may assist with plans for obese patients to attain a goal weight or provide support for underweight patients to ensure adequate nutritional intake. Their role may differ depending on the organ, for example assisting with diabetic diet is a common need for kidney transplant recipients whereas addressing malnourishment in cirrhotic patients is more common in liver transplant.

The importance of the histocompatibility lab and its active role in solid organ transplant cannot be over emphasized. It plays a crucial role for pre-transplant for assessment of organ compatibility and final crossmatch before surgery. Special medical situations need particular attention before finalizing the crossmatch before surgery such as lupus, HIV, use of certain immunosuppressive medications, and patients who are highly sensitized. The HLA director and team must be thorough and meticulous. They also play a significant role post-transplant in patient management by analyzing antibody profiles for the presence of HLA and non-HLA antibodies that put the graft at risk. Again, team development will take time and collaboration with other institutions will help in achieving the goal.

Developing an organ recovery team and network is a time-consuming process and will require strategic planning and commitment. Highly specialized teams are mobilized when a deceased donor is identified. This process development can be revisited when deceased organ donation becomes a reality in Pakistan.

In addition to staff development there are certain processes that should be practiced meeting international standards. These processes include, but are not limited to:

1. Multi-disciplinary rounds
2. Multi-disciplinary selection committee
3. Multi-disciplinary living donor selection committee
4. Mortality & Morbidity conference (regarding immediate surgical complications)
5. Focused - Quality Assurance and Performance Improvement (QAPI) meeting
6. Physicians Group meeting

The frequency of these meetings can be determined based on program requirements.

CONCLUSION

Transplant program development will require extensive commitment and sacrifice. The biggest challenge will be to start performing deceased donor transplants and

standardizing the existing living donor transplantation programs to improve outcomes. It is a daunting task but can be achieved with proper leadership and responsibility. There will be hurdles, setbacks, and delays, but these can be overcome with perseverance, focus and hard work. Those who have been granted the opportunity to train at the highest levels abroad can participate and provide support in this noble cause. An initial step can be to strengthen existing institutions already in place, to support physicians and leaders who are managing transplant programs with minimal resources. Then expanding the effort in starting new transplant programs throughout Pakistan. This is our human responsibility and debt to our nation.

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REFERENCES

1. Population: the numbers | Population Matters. Accessed November 10, 2021. https://populationmatters.org/population-numbers?gclid=Cj0KCQiA-K2MBhC-ARIsAMtLKRuaH0SZHb3PqVoF2aK4lfUMH4sYRzH5bO8-9wtkIX4v3TQqLtgIQ4aAkD_EALw_wcB
2. World Bank Open Data | Data. Accessed November 10, 2021. <https://data.worldbank.org/>
3. Pakistan Renal Data System. Accessed November 10, 2021. <https://pkrds.com/faq.php>
4. Rizvi SA, Anwar Naqvi SA. Saudi Journal of Kidney Diseases and Transplantation. *Saudi J Kidney Dis Transplant.* 1996;7(4):404. Accessed November 10, 2021. <https://www.sjkdt.org/article.asp?issn=1319-2442;year=1996;volume=7;issue=4;page=404;epage=408;aulast=Rizvi>
5. Rizvi SAH, Manzoor K. Saudi Journal of Kidney Diseases and Transplantation. *Saudi J Kidney Dis Transplant.* 2002;13(3):376. Accessed November 10, 2021. <https://www.sjkdt.org/article.asp?issn=1319-2442;year=2002;volume=13;issue=3;page=376;epage=379;aulast=Rizvi>
6. Jafar TH. The growing burden of chronic kidney disease in Pakistan. *N Engl J Med.* 2006;354(10):995-997. doi:10.1056/NEJMP058319
7. Home | USRDS. Accessed November 10, 2021. <https://www.usrds.org/>
8. Garcia-Garcia G, Jha V. CKD in disadvantaged populations. *J Bras Nefrol.* 2015;37(1):14-18. doi:10.5935/0101-2800.20150003
9. Sindh Institute of Urology and Transplantation. Accessed November 10, 2021. <https://siut.org/index.php>
10. Steering Committee of the Istanbul Summit. Organ trafficking and transplant tourism and commercialism: the Declaration of Istanbul. *Lancet (London, England).* 2008;372(9632):5-6. doi:10.1016/S0140-6736(08)60967-8
11. H Rizvi SA, Anwar Naqvi SA, Zafar MN, et al. Pakistan Abolishes Kidney Market and Ushers in a New Era of Ethical Transplantation. *Int J Organ Transplant Med.* 2010;1(4):193. Accessed November 10, 2021. </pmc/articles/PMC4089237/>
12. Moazam F, Jafarey A. Pakistan's experience with kidney transplantation and trade: a call for international solidarity. *Indian J Med Ethics.* 2014;11(3):156-162. doi:10.20529/IJME.2014.042
13. Shroff S. Challenges in setting up of a deceased donor transplant program in South Asia. *Indian J Transplant.* 2018;12(3):161. doi:10.4103/IJOT.IJOT_34_18
14. Rizvi SAH, Naqvi SAA, Zafar MN, et al. A renal transplantation model for developing countries. *Am J Transplant.* 2011;11(11):2302-2307. doi:10.1111/J.1600-6143.2011.03712.X
15. Rizvi SAH, Naqvi SAA, Zafar MN, Akhtar SF. A kidney transplantation model in a low-resource country: an experience from Pakistan. *Kidney Int Suppl.* 2013;3(2):236. doi:10.1038/KISUP.2013.22
16. Your access to this site has been limited by the site owner. Accessed November 10, 2021. <https://unos.org/>
17. Rizvi SAH, Naqvi SAA, Zafar MN, et al. Living related renal transplants with lifelong follow-up. A model for the developing world. *Clin Nephrol.* 2010;74 Suppl 1(SUPPL1). doi:10.5414/CNP74S142