Review Article

Kidney Transplantation in India—Past, Present and Future

Abstract

Kidney Transplantation is universally recognized as the best treatment option for patients with kidney failure. The first successful kidney transplant in India was done on 2nd Feb 1971 at Christian Medical College (CMC) Vellore by Dr. Mohan Rao and Dr. K. V. Johny, 17 years after the first kidney transplantation between identical twins in Boston, USA. It marked the beginning of a new era in kidney care in India. This article reviews the history of transplantation, its current status and looks forward to the future while discussing the issues and progress made in India.

Keywords: *Kidney transplantation, immunosuppression, Immunology, Paired exchange, Ethical issues*

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Introduction

Kidney transplantation is universally recognized as the best treatment option for patients with end-stage kidney disease (ESKD). The first successful kidney transplant in India was done on February 2, 1971, at Christian Medical College (CMC), Vellore, by the team led by Dr. Mohan Rao (surgeon) and Dr. K. V. Johny (nephrologist), 17 years after the first kidney transplantation between identical twins in Boston, USA. It marked the beginning of a new era in kidney care in India.[1,2]

Transplantation activity picked up across the country in the 1970s and 1980s [Table 1]. Given that kidney transplantation is transformative for patients with kidney failure, a condition whose burden is projected to grow over the coming decades,[3] it is time to reflect upon the current status of kidney transplantation in India.

India has around 600 kidney transplant centers. Out of these, 75 are in the public sector and the rest in the private sector. A total of 13,642 kidney transplants were done in 2023, 11,791 from living donors and 1,851 from deceased donors; three of these were donated after cardiac death (DCD) by Dr. Anil Kumar (NOTTO). For a country of around 1.5 billion people with an ESKD burden of at least 200,000 patients every year, these numbers are tiny, indicating the huge gap between demand and supply.[4]

Transplantation of Human Organs Act

The Transplantation of Human Organ Act (THOA) provides a strong legal and ethical framework for organ donation and transplantation in India. The Act were promulgated in 1994 and amended in 2008 and 2011. The Transplantation of Human Organs and Tissue Rules were formulated in 2014.[5] The aim of the THOA was to promote deceased donor transplantation and prevent illegal commercial transplantation. The 2011 amendment paved the way for setting up the National Organ and Tissue Transplantation Organization (NOTTO), which collects data from all states and union territories and submits them to the Global Observatory on Donation & Transplantation (GODT).[6]

Establishing a nationwide online organ transplant registry under NOTTO remains a work in progress. Multiple attempts at developing a national organ registry have not been successful. Even 50 years after the first transplant, it is alarming that we do not have a national database of kidney transplantation outcomes in the country.

Deceased donor transplantation

Deceased donor transplantation (DDT) received a formal sanction with the promulgation of THOA. The uptake of DDT has been variable across the country. Mohan Foundation, a nongovernmental organization led by Dr. Sunil Shroff, has played a pivotal role in promoting DDT

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Table 1: Transplantation in the 1970s and 1980s in India

Year	Centre	Nephrologist	Surgeon
1971	CMC Vellore	Dr. K V Johny	Dr. Mohan Rao
1972	AIIMS New Delhi	Dr. K K Malhotra	Dr. Inder Dhawan
			Dr. B M L Kapoor
1974	PGIMER Chandigarh	Dr. K S Chugh	Dr R V S Yadav
1974	Jaslok Hospital (Mumbai)	Dr. Chacko Kuruvilla	Dr. B.N Colabawalla
			Dr. F P Soonawalla
1977*	Jaslok Hospital & Nanavati Hospital (Mumbai)	Dr. Chacko Kuruvilla	Dr. B.N Colabawalla
		Dr. Bhupendra Gandhi	Dr. F P Soonawalla
			Dr. K N Dastur
1979	Lakeside Hospital (Bangalore)	Dr. Talwalkar	Dr. Dilip Javali
			Dr. Ajit Huilgol (helped by Dr. Shyam Joshi, & Dr. M H Kamath from Mumbai)
1980	Mulji Bhai Urology & Nephrology Institute, Nadiad	Dr. Mohan Rajapurkar	Dr. Mahesh Desai
			Dr. Virender Desai
1981	Green Hospital, Hyderabad		Dr. S Sahariah
1982	Osmania Hospital, Hyderabad	Dr. Gopal Krishan	Dr. Rangnath Rao
		Dr. Girish Narayan	Dr. B V Rama Raju
		Dr. Raja Mallaih	
1984	Institute of kidney disease at Civil Hospital Ahmedabad	Dr. H L Trivedi	
1984	Sir Ganga Ram Hospital	Dr. D S Rana	Dr. S Sahariah
1984	Apollo Chennai Hospitals	Dr. M K Mani	Dr. Subramaniam
		Dr. K S Ramalingam	
1985	Stanley Hospital, Chennai	Dr. Muthu Jairaman	Dr. Subramaniam
1985	Guest Hospital, Chennai	Dr. C M Thiagarajan	Dr. C Ramachandra,
			Dr. Jai Chandran
1985	Vijaya Hospital, Chennai	Dr. Rajan Ravichandran	Dr. P B Sivaraman
			Dr. Subramaniam
1985	Govt. Medical College, Calicut	Dr. Thomas Mathew	Dr. Roy Challi
1986	Madras Medical College Chennai	Prof. M A Muthusethupathi	Dr. Subramaniam
1989	SGPGIMS, Lucknow	Dr. Vijay Kher	Dr. Mahendra Bhandari
		Dr. R K Sharma	Dr. Anant Kumar
		Dr. Amit Gupta	Dr. Rajesh Ahlawat

*Two kidneys flown from USA in 1977 by Dr. Samuel L Kountz, Dr. Gobind Laungani, and Dr. TKS Rao to Mumbai. One transplanted to a recipient in Jaslok Hospital and one in Nanavati Hospital.

through education, training, and coordination initiatives. NOTTO has now taken up the leadership role in increasing awareness about organ donation and regulating transplantation, along with SOTTO (state) and ROTTO (regional) organizations.[6,7]

Currently, the Southern states are ahead of the rest of the country in the implementation of DDT programs, with Telangana, Karnataka, and Tamil Nadu being the top of the list, followed by Gujarat, Maharashtra, Rajasthan, Chandigarh, and Kerala. It must be pointed out that even though ahead of others, these states service a tiny minority of their populations in need and are far behind most of the leading countries in DDT per million of the population. Jeevandan in Telangana was ranked first among the various organ transplantation programs in the country this year. Around 1400 donations have been made to date since the inception of the program in 2013, and more than 5000 organs have been retrieved. There were 200 donations in 2023 and 104 donations in 2024 to date. The Transplant Authority of Tamil Nadu (TRANSTAN) retrieved 678 organs from 168 donors in 2023. Among the Union Territories, Chandigarh excelled at organ donation, with 41 organ donors in 2022. However, the national organ donation rate is around 1/pmp (donors per million population), which needs to increase substantially to meet the needs of ESKD patients in the country.

There is a need for greater awareness and education about the importance of organ donation. The major barriers to DDT are the failure to transport trauma victims quickly and the lack of intensive care units (ICUs). ICU doctors are not

engaged, there is public distrust, transplant coordinators are scarce and poorly paid, and hospitals do not follow the stipulation that all ICUs must identify and report brain deaths. Large-scale awareness campaigns need to be implemented in order to increase deceased organ donation. Steps should be taken to build public trust by optimally utilizing public health systems. Police personnel need to be sensitized to make the organ donation process smoother in medicolegal cases. Increasing the number of organ retrieval centers by making registration of non-transplant centers mandatory for retrieval is essential. Sensitizing the ICU doctors and staff in this regard and counseling by the transplant coordinator are also very important. Transparency, public trust, a just and equitable distribution system, and effective regulations are essential in improving deceased organ donation. "One nation, one organ" means the same laws for organ transplantation across the country, and one national waitlist for organs needs to be implemented sooner rather than later. This will also avoid varying practices in different states and regions and enhance uniformity and standardization of practice across the centers. Several practical challenges can be foreseen, that need to be sorted out.

Advances in kidney transplant surgery

Kidney transplant surgery for donors and recipients had started as an open surgical procedure. By 2000, many centers had adopted laparoscopic donor nephrectomy as a minimally invasive surgery for donors, which is now the standard practice in most transplant centers. Drs. Rajesh Ahlawat at Medanta Hospital and Pranjal Modi at the Institute of Kidney Diseases in Ahmedabad initiated robotic transplant surgery for recipients in 2014,[8,9] and its popularity has increased over time.[10]

Immunological tests—changing scenario

In the early days of kidney transplantation, complement-dependent cytotoxicity crossmatch (CDC-XM) was the only immunological test. A few centers did low-resolution human leukocyte antigens (HLA) typing using serological methods. There were few specialized immunology laboratories. Dr. Balakrishnan from the Army Hospital used to provide support for CDC-XM in the late 1970s before moving to the University of Cincinnati, USA. Over time, centers and labs have incorporated advances in the technology of immunological evaluation.

HLA typing

Low-resolution HLA typing by serological methods is still the most commonly used method for HLA typing. High-resolution HLA typing is available in many standard national laboratories, essentially at a similar cost to low-resolution HLA typing. The latter is critical to the interpretation of donor-specific antibody (DSA) testing using the Luminex platform, and should be the norm for HLA typing of donors and recipients.[11]

Antibody testing in transplantation

For almost 40 years, CDC-XM, described by Drs. Terasaki and Patel in 1967, was the only test done to look for anti-donor antibodies in the recipient.[12] A negative CDC-XM was considered to be a must before proceeding with kidney transplant surgery and continues to be done in the current era in most transplant centers.[13]

Flow cytometric crossmatch (FC-XM), a sensitive technique that enables the detection of the antibody of all immunoglobulin (IgG) isotypes, including both complement-fixing and noncomplement-fixing, started in India in 2010. The combination of FC-XM with panel reactive antibody (PRA) (Luminex) and single-antigen bead (SAB) assays is highly sensitive and specific for identifying clinically significant DSAs, making CDC-XM redundant.[13] The use of SAB testing is limited to select centers and is usually employed only if FC-XM is positive or in high immunological risk and sensitized patients.

Cost-cutting attempts to find a substitute for these techniques have led to using tests like Lysate-based crossmatch on the Luminex platform. However, these have high false positive and negative rates. Given that they are neither reliable nor reproducible, there is no place for these tests in current-day practice.[14]

Technological advances in immunological evaluation, like FC-XM and SAB Luminex assays, have played important roles in improving outcomes in kidney transplantation. It is thus imperative that well-standardized assays are utilized for daily clinical practice.[13,15,16] Cost is often mentioned as a barrier, but these tests are significantly cheaper than the prices even ten years ago and are cost-saving in the long run.

Immunosuppression

The modern era of immunosuppression started in India in the late 1980s with the introduction of cyclosporine. Early acute rejection (AR) rates came down and transplantation across the HLA barrier picked up. Initial practice limited cyclosporine use for one year, primarily due to cost considerations and the fear of long-term chronic cyclosporine toxicity. This led to High rates of acute rejections after withdrawal,[17] Leading to a change in practice. Generic tacrolimus formulations were introduced in 2006 and quickly overtook cyclosporine as the calcineurin inhibitor (CNI) of choice. Currently, generic tacrolimus, mycophenolate, and steroids are the most common maintenance immunosuppressive agents. The use of mammalian target rapamycin (mTOR) inhibitors remains limited.[18,19]

Therapeutic drug monitoring, uncommon in the initial years, is now universally available. Normal trough level targets are 8–12 ng/mL in the first three months, 7–10 ng/

mL in three to six months, and above 5 ng/mL (4–6 ng/mL) beyond six months. Steroid withdrawal protocols are uncommon.[20]

Induction Therapy

Rabbit anti-thymocyte globulin (ATG) (Thymoglobulin, Sanofi) at 2–3 mg/kg and Grafalon (ATG, Neovi marketed by Zydus) at 4–6 mg/kg are used in about 50% of transplants in India. IL2RA (basliliximab) use has declined to around 10–15%, with the rest not getting any induction.[21–23]

Desensitization is used for high-risk patients with moderate anti-HLA antibody titer and ABOi transplant using rituximab, plasmapheresis, and induction agents like thymoglobulin, Grafalon, and IL2RA (mostly in ABOi transplants).[24]

Clinical Outcomes

Acute rejection

Approximately 10–15% of patients experience AR in the first year. With ATG induction, the rates have reduced to less than 10%. AR is effectively managed by intravenous (IV) steroids 250–500 mg for three to five days and ATG for steroid-resistant acute cellular rejection (ACR). The incidence of antibody-mediated rejection (ABMR) in the first year has reduced significantly with the increasing use of sensitive crossmatch techniques and single-antigen-based assays.[13,25]

Patient and graft survival

There are not many studies documenting transplant outcomes. The current one-year patient and graft survival is estimated to be around 95% and 90–95%, respectively. The five-year patient and graft survival figures are 85–90% and 75–80%, respectively, and the ten-year patient and graft survival is 70–75% and 60–65%, respectively.[1,25–27]

Graft loss

Infections and cardiovascular diseases are the most common causes of death. Chronic ABMR, AR, death with functioning graft, and recurrent or de novo glomerulonephritis are common causes of graft loss.[1,25,26]

Infections

Infections remain the leading causes of morbidity and mortality. Bacterial infections like urinary tract infection (UTI), pneumonia, tuberculosis, fungal infections, and viral infections, including cytomegalovirus (CMV) and BK polyomavirus, are common in the posttransplant period.[27–30] Apart from tuberculosis, the epidemiology, clinical presentation, and outcomes of other infections are not well-documented. The availability of sophisticated tests has reduced the overall burden of infections in the last decade.

Paired kidney exchange transplantation

Paired kidney exchange (PKE), done first in South Korea in 1991,[31] is seen as an important strategy to increase access to transplantation, which can take the form of paired exchange, three-way, four-way, or multiway transplant.[32] PKE is mainly practiced at a single-center level [Table 2].[33–37,38] Successful multiway transplants have also been reported.[38,39] The lack of a regional- or national-level registry is a barrier to scale-up. Difficulties in maintaining anonymity can lead to coercion and financial dealings. Rare instances of reneging by a donor have been reported.[32] The report by Kute *et al*. on no reneging during 17 nonsimultaneous kidney exchanges appears reassuring in this regard.[40] The THOA 2011 amendment made PKE easier. However, significant hurdles remain, such as the need for clearance from different authorization committees when participating pairs are from different states.

The NOTTO should facilitate regional and national PKE programs. PKE registries will help in increasing

Table 2: Experience of paired kidney exchange transplants from India

Study	Study period and follow-up	Patient details	Outcome and remarks
Modi *et al*., 2010[33]	2000–2009	34 pairs	PS: 76.5%
		Reason for exchange: ABO incompatible in 12 and positive crossmatch in 5 pairs	DCGS: 94.1%
Waigankar *et al*., 2013[34]	2008–2011	7 PKE	PS: 100%
	12 months	Reason for exchange: ABO incompatibility in all	DCGS: 100%
Kute *et al*., 2013[35]	2000–2012	70 PKE	PS: 81%
	2.7 years mean	Reason for exchange: ABO incompatibility in 56, positive crossmatch 14	DCGS: 90.2% (five-year survival)
Jha *et al*., 2015[36]	2010–2013	26 PKE versus 716 non-PKE	PS: 96.2%
	20 months median	All two-way PKE; reason for exchange: ABO incompatibility	DCGS: 96.2%
			BPAR: 11.5%
Kute *et al*., 2017[39]	2015–2016	77 PKE	PS: 93.5%
		Reason for exchange: ABO incompatibility in 45, sensitization in 26, better matching in 6	DCGS: 98.7%
			LDKT increased by 25% in a year due to PKE
Kute *et al*., 2017[37]	2000–2016	300 PKE	PS: 83.3%
	3 years mean	Reason for exchange: ABO incompatibility in 222, positive crossmatch in 59, better matching in 19	DCGS: 96%
		124 two-way; 14 three-way, 1 four-way, 1 six-way	

PS: Patient survival, DCGS: Death censored graft survival, PKE: Paired kidney exchange, LDKT: Living donor kidney transplantation

such exchanges. The need for multiple authorization committees' clearances in case of interstate PKE should be abolished, with clearances coming from a central committee authorized by NOTTO. Utilizing O blood group donors in the pairs can increase the donor pool. Table 2 summarizes the Indian experience of PKE transplantation in the country.[33–37]

ABO incompatible kidney transplantation

Since the first reports over 10 years ago, transplantation across the ABO barrier has become common.[41,42] Preconditioning regimens involve use of plasmapheresis (with or without IVIG) or immunoadsorption and Rituximab. In a report of 100 ABOi transplants,[43] of the graft and patient outcomes were at par with those of the compatible group, barring the initial graft loss in the first two weeks due to hyperacute rejection. The non-availability of complement inhibitor eculizumab to tackle such a crisis remains an important issue. Such transplants are also fraught with a higher risk of infection.[44,45] An Indian working group recommendation for ABOi transplant was published in 2019.[46] Table 3 summarizes the Indian experience of ABOi kidney transplant.[41,43,47–53]

Challenges and issues

Despite significant progress, the kidney transplant program in India faces many challenges.

Ethical issues

Despite the THOA—which provides legal framework for organ donation and transplantation in India being operative

Table 3: Experience of ABO incompatible kidney transplants from India

Study	Study period and follow-up	Patient details and follow-up	Preconditioning	Induction	Outcome
Ravichandran *et al.*, 2012[41]	2009–12 4 weeks to 28 months	13 ABOi	PE + IVIG Ritux	Bas	PS: 100% GS: 85% ABMR: 15%
Jha *et al.*, 2016[47]	2011–14 ABOi: 10 months ABOc- 17 months	20 ABOi versus 669 ABOc	5 pts: PE with IVIG 12 pts: DFPP 3 pts: none Ritux	ABOi: Bas ABOc: 55% Ritux, 5% ATG, 40% none	PS: 90% DCGS: 95% BPAR: 15% ABMR: 0%
Jha *et al.*, 2018[48]	2011–2017	50 ABOi	PE/DFPP/IVIG	Bas	PS: 94% DCGS: 88% BPAR: 22% ABMR: 8%
Thukral S *et al.*, 2019[49]	2014–2015 12 months	30 ABOi	PE Ritux	ATG	PS: 96.7% DCGS: 96.7% ABMR: 0%
Prabhakar A *et al.*, 2021[50]	2013–2019 26 months	100 ABOi 100 ABOc	PE Ritux	Bas/Thymo	PS: 93.3% DCGS: 73.5% ABMR: 15%
Mukherjee D *et al.*, 2021[51]	2014–2018 30 months	30 ABOi	IA		PS: 86.7% DCGS: 100% ABMR: 3%
Jha *et al.*, 2022[43]	2011–2020 33 months (median)	100 ABOi	PE + IVIG, DFPP ± IVIG, IA Ritux	Bas: 65% Thymo: 11% Grafalon: 11% None: 13%	PS: 93% DCGS: 94% BPAR: 17% ABMR: 3% Infection: 17%
Pawar N *et al.*, 2024[52]	2012–2021 29 months	195 ABOi	PE/IA Ritux	Bas/Thymo/ Grafalon	PS: 86.6% DCGS: 89.3% ABMR: 15%
Kute *et al.*, 2023[53]	2011–2022 36 months	1759 ABOi versus 33157 ABOc	IA/PE/IVIG Ritux	Bas/ATG/No induction	Mortality: 9.5% Graft loss: 7.7% BPAR: 12.6%

PE: Plasma exchange, IVIG: Intravenous immunoglobulin, DFPP: Double filtration plasmapheresis, ATG: Anti thymoglobulin, IA: Immune adsorption, PS: Patient survival, GS: Graft survival, ABMR: Antibody mediated rejection, DCGS: Death censored graft survival

since 1994—illicit organ trade and unethical practices have continued. Reports of kidney rackets operating in different parts of the country appear frequently. Despite stringent laws, enforcement and monitoring remain inconsistent across regions, and the current penalties do not seem to be a deterrent. Besides being exploitative and coercive, these incidents bring a bad name to the country's medical fraternity.[54] In addition to established centers, these transplants are also done in hidden, unhygienic places, putting both recipients and donors at risk of complications. There have been calls for legalizing unrelated transplants through a regulated system from Western countries.[55] We believe this would be going down a slippery slope where the solution may become worse than the disease. Moreover, it will put an end to altruistic deceased donors and living-related donor transplantation and may become a social catastrophe.

Gender disparity

The gender disparity between kidney donors and recipients in India has been highlighted in scientific literature as well as in the lay press. Over 70% of the transplant recipients are males, whereas females constitute over 70% of the donor population. In spousal transplants, over 90% of donors are females. This reflects the general social disadvantage females face in our country.[56]

Donor follow-up

The trepidation and dilemma of doing a donor surgery for the good of someone else in the first transplant in the world was highlighted in Dr. Murray's Nobel Prize acceptance speech. Donor surgery has a low mortality (0.03–0.01%), but even one death is a death too many.[57] Given the lack of high-quality, mass-based dialysis programs and a weak deceased donor program, there is a great deal of reliance on living donors. Quite often, donors with comorbidities (e.g., elderly and those with hypertension, prediabetes, diabetes, obesity, cardiovascular disease, marginal kidney function, and impaired mental health) come forward to donate. There is a need to develop a consensus for acceptable risk and document short- and long-term follow-up data of living donors for the safety of donor surgery for all living donors.

India as a transplant tourism hub

India is emerging as a medical tourism destination for kidney transplants, especially for low- and lower-middle-income countries. With the availability of state-of-the-art technology, skilled manpower, low-cost surgery, and comparable success rates with the Western world, India has all the right ingredients. However, it becomes essential to establish an enhanced legal and ethical framework so as not to allow unethical commercial transplants before we establish ourselves as a transplant tourism hub.

Kidney transplantation in India has made significant advancements in medical, surgical, and immunological work-up technology and practice, leading to improved clinical outcomes. However, the current transplant ecosystem faces challenges in relation to donor availability, ethical issues, and legal enforcement. Despite these challenges, leading transplant centers across the country continue to drive progress and provide hope to thousands of patients in need of life-saving kidney transplantation. One hopes the challenges will be resolved soon rather than later.

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Conflicts of interest

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