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Review Article

Nephrology and kidney transplantation in India: Past, present and future



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ABSTRACT

Chronic kidney disease (CKD) has been recognized as a major global public health problem. The approximate prevalence of CKD in India is 800 per million populations (pmp). Kidney transplantation is considered as the best therapeutic modality for patients suffering from end stage renal disease (ESRD). Transplantation started in 1953 in Europe and USA and in India it started in 1965. The awareness of deceased donor organ transplants, cross-over transplants and other organs like liver and heart is also gradually increasing with Tamil nadu leading the country in deceased donor organ transplants. The alternative to post-transplant immunosuppression and associated problems is 'transplant tolerance' which means stable graft function with no immunosuppression while keeping immune system of the host intact. We at Ahmedabad have pioneered the technique of in vitro generation of human adipose tissue-derived mesenchymal stem cells (AD-MSC) and T-regulatory cells. Once again we have pioneered (in the world) the infusion of these cells along with hematopoietic stem cells in renal allograft recipients. Abrogation of antibodies using Bortezomib again established by our group in Ahmedabad which is now universally being adapted has improved renal transplant outcomes. This review briefly takes the reader to evolution of nephrology and kidney transplantation in India and shows that we have bright future!

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The evolution of Nephrology as a subspecialty branch in India dates back to early seventies. I remember my old days as a faculty of Nephrology and Renal Transplantation from McMaster University in Canada. Indian physicians coming to international meetings had almost no knowledge on the subject till 1970. I came back to India in 1977 to establish an institute for kidney diseases for my people in India and started my career in my own alma mater in B.J. Medical college, Ahmedabad. Those were the days when we performed dialysis using catheters because dialysis facilities were yet to develop in India. Since then much water has passed under the bridge!

Chronic kidney disease (CKD) has been recognized as a major global public health problem.¹ The overall magnitude and pattern of CKD in India has been studied sporadically.^{2–4} There are no national or regional reports on incidence or prevalence of either CKD or end-stage renal disease (ESRD) in India. The approximate prevalence of CKD in India is 800 per million population (pmp), and the incidence of ESRD is 150–200 pmp. The contribution of kidney diseases to death in India is not known but is believed to be the third major killer of its population next to cancer and heart diseases. The reason for lack of availability of information on kidney failure in India

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is that we do not have established program to manage CKD patients or even to collect data.² Patients from financially privileged strata consult private hospitals/physicians and subsidized/free care is provided through the government centers or hospitals to other patients. Sometimes a shortage in the number of publicly funded specialized hospitals forces patients to seek care in expensive private hospitals. Unfortunately since vast majority do not have personal resources for these amenities hence die of ESRD. In this background, Nephrology has slowly and steadily picked up in India and today in 2014, more and more Physicians are volunteering to be trained as Nephrologists and many of them are becoming good transplanters.

Once a patient meets with ESRD, the options are dialysis or transplantation. The former being a makeshift arrangement to keep the patient alive, proves expensive. Secondly the procedure of dialysis involves opening up of vascular system due to arterio-venous shunts required to carry out exchange of blood in the form of removal of toxic products from the blood and reinfusing the cleansed blood into the circulation through mechanical means. This opening up of central lines jeopardizes life of the patient due to associated complications of hypertension, electrolyte disturbances, diabetes and infections like hepatitis B/C or fungal or bacterial infections. The best option for such a patient especially in developing country like India with poor general hygiene standards is, therefore transplantation.

Kidney transplantation was successfully registered to have been performed by John P. Merrill and Joseph Murray in Peter Brent Brigham Hospital in Boston in identical twins and in Paris by Jean Hamburger from sister to brother in 1953. Indians of the modern day have not lagged far behind. Looking to the milestones of development of Nephrology, transplantation has evolved phenomenally in India. If we glance at the organ transplantation scenario in India, the concept of organ transplantation as a therapy for replacement of non-functioning organs originated in mythological medicine in the twelfth century B.C. Lord Ganesha, revered as a God of wisdom and vanquisher of obstacles is an example of the very first xenotransplantation performed by Lord Shiva using an elephant's head in world history. This has been followed by several similar examples in many other civilizations round the world involving use of limbs, heart and the spirit. In the sixth century B.C., Sushruta, our ancient Indian surgeon introduced the technique of skin autografts for rhinoplasty. Several Greek, Italian and other surgeons from many other parts of the world followed suit. Their efforts provided a tremendous insight into the likely surgical problems to be encountered in organ transplantation including the anastomosis of blood vessels. All aspects of surgical technique were mastered by generations of surgeons till date.

The immunological development in transplantation evolved with the discovery of the co-dominant major histocompatibility gene complex that controlled transplant survival between inbred mouse strains. The recognition by body cells of "self from non-self" and attempts to overcome the same, has been the greatest advance noticed in the field of transplantation immunology. In keeping with progress made in the rest of the world, in India too, attempts were made towards human organ transplantation. The initial experimental kidney

and liver transplants were attempted in dogs by Dr. PK Sen and his team from King Edward VII Memorial (KEM) Hospital from Mumbai in the 1950s. The first ever human kidney transplant performed in India was done at the KEM Hospital in Mumbai in May 1965, using a cadaver donor in a non-renal failure patient who had hypernephroma. The second kidney transplant in April 1966 – a deceased donor once again – was carried out by the same team in a case of CRF. This was followed by a similar cadaver (deceased donor) organ transplant by Dr. Udapa and his team from BHU, Varanasi. The detailed report of the first two transplants has been published in the Indian Journal of Surgery in February 1967. The first patient died on the 11th post-operative day following acute myocardial infarction, with a functioning graft. The second patient died on the 3rd post-operative day due to bilateral pneumonic consolidation. The first successful live donor renal transplant in India was done at the CMC Hospital, Vellore in January 1971. Johny and Mohan Rao reported an account of their first five successful renal grafts in Indian Practitioner in July 1972. Though this was almost 17 years after the first "identical twin" transplanted by Murray et al, in 1954, a successful start had been made in the field of human renal transplantation in India by the Vellore team. They concluded that renal transplantation was feasible in India and has a definite future. They had however warned that inadequately and improperly planned attempts at transplantation might lower the morale of the patients as well as the public. Since then several thousand transplants have been done in our country, but in the absence of a proper registry, it has been impossible to ascertain the exact number of transplants done so far in India. In fact we at G. R. Doshi and K. M. Mehta Institute Of Kidney Diseases & Research Centre (IKDRC) – Dr. H.L. Trivedi Institute Of Transplantation Sciences (ITS) in Ahmedabad have maintained the record of performing the highest number of kidney transplants in India for the last at least 15 years. We have broken our own past records and in the year 2013, we performed 400 kidney transplants. The awareness of deceased donor organ transplants, cross-over transplants and other organs like liver and heart is also gradually increasing with Tamil Nadu leading the country in deceased donor organ transplants.

However, all the patients have to be maintained on life-long immunosuppression to prevent the rejection of the grafted organs. All immunosuppressive medications have toxic side effects of suppressing the general immune response of the recipient.⁵ This leads to increased susceptibility of the patients to bacterial, viral and fungal infections. Once a patient contracts these infections, morbidity and mortality are very high. The other risk these patients face is that of malignancies. Apart from infections and malignancies there is multitude of problems related to medications ranging from alopecia to hirsutism, bone metabolism and endocrine metabolism disorders. Post-transplant diabetes is one such common problem, and in spite of administration of adequate immunosuppressive medication, eventually the graft is lost to chronic attrition.⁶ The standard cost of care in most of the centres in India for these patients costs anywhere from Rs. 5000 to Rs. 30,000 per month.

The alternative to post-transplant immunosuppression and associated problems is 'transplant tolerance' which means stable graft function with no immunosuppression while

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