

Deceased-donor renal transplantation program in India

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The crude and age-adjusted incidence rates of end-stage renal disease are estimated to be 151 and 232 per million population, respectively, in India.¹ Chronic kidney disease in India is predominantly due to diabetes mellitus and hypertension, as shown by data from the Indian CKD registry, comprising 36,000 patients. The majority of the end-stage renal disease patients (>90%) in India and in other South Asian countries die within months of diagnosis, as renal replacement therapy is not affordable or not available.² The rate of renal transplantations performed yearly in India translates to 3.25 per million population; the deceased-donation rate is 0.08 per million population per year.³ Since the promulgation of the Transplantation of Human Organs Act of 1994 (THOA), nongovernmental organizations in partnership with the state governments have expanded the deceased-donor transplantation program. Organizing a nationwide deceased-donation program in India will always be a logistical challenge, as many towns and villages lack doctors and hospitals with infrastructure for renal care. India spends 5.2% of its gross domestic product (US\$1.237 trillion in 2007) every year on health-care coverage, with only 0.9% coming from government contribution. There are regional disparities, with the southern and western regions of the country having better industrial growth and literacy rates and better infrastructural support in the way of hospitals and doctors to support deceased-donor programs.

Current state of deceased-donor renal transplantation program

After the passage of THOA by the Indian parliament, the deceased-donation program was initially confined to half a dozen hospitals, with donation continuing in a sporadic manner, and since then has expanded to about 20 multi-specialty hospitals with better infrastructure. The organs that were not used by the harvesting hospitals were offered to other hospitals.⁴ In 1999, a meeting of six such hospitals that were regularly doing deceased donations in Tamil Nadu was arranged by a nongovernmental organization body called the Multi Organ Harvesting

Aid Network (MOHAN), and the six hospitals decided to form a formal organ-sharing network in the country.⁵ A similar sharing network was started by the same nongovernmental organization in the neighboring state of Andhra Pradesh in 2003 and employed grief counselors who could explore the possibility of organ donation. In both states MOHAN has facilitated the sharing of over 400 deceased-donor organs. This is nearly one-third of the total deceased transplants (about 1400) done so far in India. The principles of the sharing network have been to not waste organs; to use them like a national resource; and to utilize them anywhere in the country where there is a needy patient. This has resulted in organs being sent by flights to Delhi, Hyderabad, and Bangalore from Chennai when there were 'no takers' for livers or kidneys in the state. In the states of Gujarat and Maharashtra, more than 300 deceased donations have taken place in the past 10 years. The Zonal Transplant Coordination Committee in Maharashtra has also evolved a sharing network for organs based on a patient point system. However, neither Maharashtra nor Gujarat share their organs with other neighboring states.

More recently, the Department of Health of the state government of Tamil Nadu decided to network all the 54 hospitals in its state that have a license for organ transplantation and to promote the deceased-donation program in the state. The four states of Tamil Nadu, Andhra Pradesh, Gujarat, and Maharashtra are leading in deceased organ donation, with a donation rate of 0.3 per million population in comparison with the national average of 0.08 per million population.⁶ The government of Tamil Nadu regulated a program of deceased-donor transplantation for the first time by appointing a convener and producing a central registry for organ sharing (<http://www.tnos.org>). As of 2009 this initiative has led, in a year, to the procurement of 140 organs from 40 deceased persons; these organs were effectively shared through meaningful public-private partnership. The government-run hospitals in the south have ensured access to deceased-donor organs to the poorest of the poor

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free of cost through this network when the kidneys were transplanted in the government facility. The Ministry of Health and Family Welfare of the government of India has pledged US\$160 million to establish organ procuring and transplant centers at the national, regional, and state levels to streamline organ transplantation in the country.

The overall potential of organ donation following brain death in India is extremely high. The number of deaths due to road traffic accidents has increased in recent years and exceeds 110,000 per year. It is estimated that 67% of such deaths occur due to brain death.⁷ In a recent monthly death audit of data of a government general hospital in Chennai, the number of patients with brain death was found to be more than 100 (J.M., unpublished data). If the current donation rate were pushed from 0.08 to 1 per million population, it would provide all the livers, hearts, and lungs that are required in the country and to some extent satisfy the kidney shortage. It is highly probable that the four southern states will reach a deceased-donation rate of 1 per million population in the next two to three years, given the current organ donation rate.⁶ Most surveys done in India indicate a positive attitude toward organ donation. India is the birthplace of the major religions of Hinduism, Jainism, Sikhism, and Buddhism, and none of these religions has set a barrier to organ donation. A recent audit has shown one-year graft survival of 90% in the state of Tamil Nadu after deceased donation. Kidneys harvested from two cobra-bite victims were successfully transplanted in four adult recipients—three of them type 2 diabetics—in 1996 and 1999 in Chennai. Two of the diabetic recipients survived for 16 and 22 months with functioning grafts, one patient was lost to follow-up after 2 years, and the third recipient was alive and well 13 years and 6 months after transplantation.

Shortcomings of deceased-donor transplantation Grief counselors are not available in the majority of the centers where counseling is needed for the families of brain death victims. Hence the doctors themselves may have to play the dual role of grief counselor and physician in charge of the patient. Presensitization is hardly ever assessed in patients on the waiting list for deceased-donor transplantation. The majority of the centers performing deceased-donor transplantation do not have facilities for cross-matching techniques in case of sensitized recipients, and a basic complement-dependent cytotoxicity is the laboratory tool for cross-matching between the recipient and the donor. Because of transportation problems, recipients who are available in the vicinity or a short distance from the transplant center have better access to deceased-donor transplantation compared with those living in the remote corners. Potentially life-saving induction agents such as interleukin-2 receptor antibodies and polyclonal antibodies are expensive, and hence the majority of the patients on the recipient list, who are self-paying, cannot afford them. Patients must bring upfront cash for hospitalization and management, as fewer than 15% have full reimbursement or insurance coverage. In a country where the living-donation program so far has been the accepted norm, a deceased-donation transplant often throws up challenges in early management of recipients with delayed graft function, dialysis, and prolonged hospital stay. Prospective recipients who are diabetic and have underlying coronary artery disease may not have had a chance to undergo full evaluation, and this is likely to increase morbidity and mortality in comparison with an elective live-donor transplantation. Human leukocyte antigen matching for class I and class II antigens in order to avoid

Table 1 | Price comparison of original and generic drugs available in the Indian market

Drug	Introductory price (US\$)	Current price (US\$)	Generic price (US\$)
Rituximab, 500 mg	1800	1200	1000
Mycophenolate mofetil, 500 mg	2.40	1.12	0.80
Daclizumab, 5 doses	3500	2500	None
Cyclosporine microemulsion, 100 mg	None	2.20	1
Basiliximab, 2 doses	2880	2000	None
Everolimus, 0.25 mg	None	1.44	None
Tacrolimus, 1 mg	None	None	0.54
Sirolimus, 1 mg	6.50	5	2
Equine anti-thymocyte globulin	None	1700	800
Thymoglobulin, 25 mg	230	187	None
Valganciclovir, 450 mg	15	9.60	4.90

mismatch is rarely performed because of time constraints and unavailability of resources and facilities in certain centers.

Support from Indian pharmaceuticals and availability of immunosuppressive agents

The Indian pharmaceutical industry has shown robust growth in the past decade by manufacturing cheaper immunosuppressive agents that are not inferior in pharmacokinetics and pharmacodynamics to the original brands. A cost comparison of the immunosuppressive agents is given in Table 1. This initiative by the Indian pharmaceutical industry has often forced the multinationals that produce the brands of microemulsion forms of cyclosporine, tacrolimus, mycophenolate mofetil, and sirolimus to bring down their prices to withstand the competition. Immunosuppressive agents of Indian origin, because of their quality and low cost, are widely used in Africa, Latin America, Russia, and Eastern Europe in addition to Asia. Therapeutic drug monitoring is available in the major cities, and the results are provided within 24–48 hours. However, the cost of drug-level monitoring can be prohibitive (US\$74.50 for sirolimus, US\$15.50 for tacrolimus, US\$19.70 for cyclosporine), and hence it is limited in the tailoring of immunosuppressive agents. As a cost-effective measure, CYP3A4 inhibitors, including diltiazem and

ketoconazole, are used to increase the blood levels and hence reduce the cost of immunosuppression. Immunosuppressive drugs are given free of cost in the state government-run hospitals in some southern states, such as Tamil Nadu.

Benefits in terms of good graft function, improved quality of life, reduced medical expenses for deceased-donor transplantation, and cheaper immunosuppressive agents have led to the offering of renal transplantation to a wider group of patients, thus avoiding selection bias depending on socioeconomic status.

DISCLOSURE

All the authors declared no competing interests.

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