



ISOT Newsletter

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Guest Editorial

Advancements, Challenges, and Future Prospects of Uterine Transplantation in India



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Dear Colleagues,

It gives me great pleasure and a sense of responsibility to contribute to the newsletter of the Indian Society of Organ Transplantation (ISOT). As a uterine transplant surgeon, I am honoured to share thoughts and reflect on India's striking development in uterus transplantation. This extraordinary journey, distinguished by a convergence of medical knowledge, technological innovation, and human spirit, has exposed both the road ahead and the problems that lay ahead.

Uterine transplantation (UTx) represents an innovative surgical technique offering renewed hope to women facing absolute uterine factor infertility (AUI), which arises from the absence or malfunction of the uterus. Globally, AUI impacts around 1 in 500 women, and in India, it constitutes 20% of all female infertility cases.

UTx involves the intricate procedure of transferring a healthy uterus from a living or deceased donor to a recipient who has undergone in vitro fertilisation (IVF) and embryo implantation. The recipient subsequently carries the pregnancy to term, culminating in a

caesarean section delivery. Typically, the transplanted uterus is removed after one or two successful pregnancies or upon the recipient's decision to cease further childbearing.

UTx is a multifaceted and demanding undertaking that necessitates a collaborative effort from a multidisciplinary team comprising gynaecologists, transplant surgeons, immunologists, anaesthesiologists, psychologists, ethicists, and nurses. The procedure also entails notable risks and financial commitments for both the donor and the recipient, encompassing surgical complications, infections, potential rejection, bleeding, thrombosis, and the need for immunosuppression.

Potential donors for UTx are typically women closely related to the recipient, and they can be either living or deceased. However, practical challenges arise when considering deceased donors. Donors must be under the age of 50, and their uterus must have a track record of successful pregnancies. It is vital to highlight that obtaining the uterus from a deceased individual increases the likelihood of organ rejection.

In the earliest cases, retrieving the uterus used to take nearly 13 hours, primarily due to open surgery procedures. However, with the introduction of laparoscopic techniques, this surgical duration has been significantly reduced to approximately six hours (Figure 1). Presently, minimally invasive surgery, including robotic procedures, has become the standard protocol. As laparoscopic suturing of the vasculature becomes more practical, uterus transplant recipients may only require a single procedure in the future.

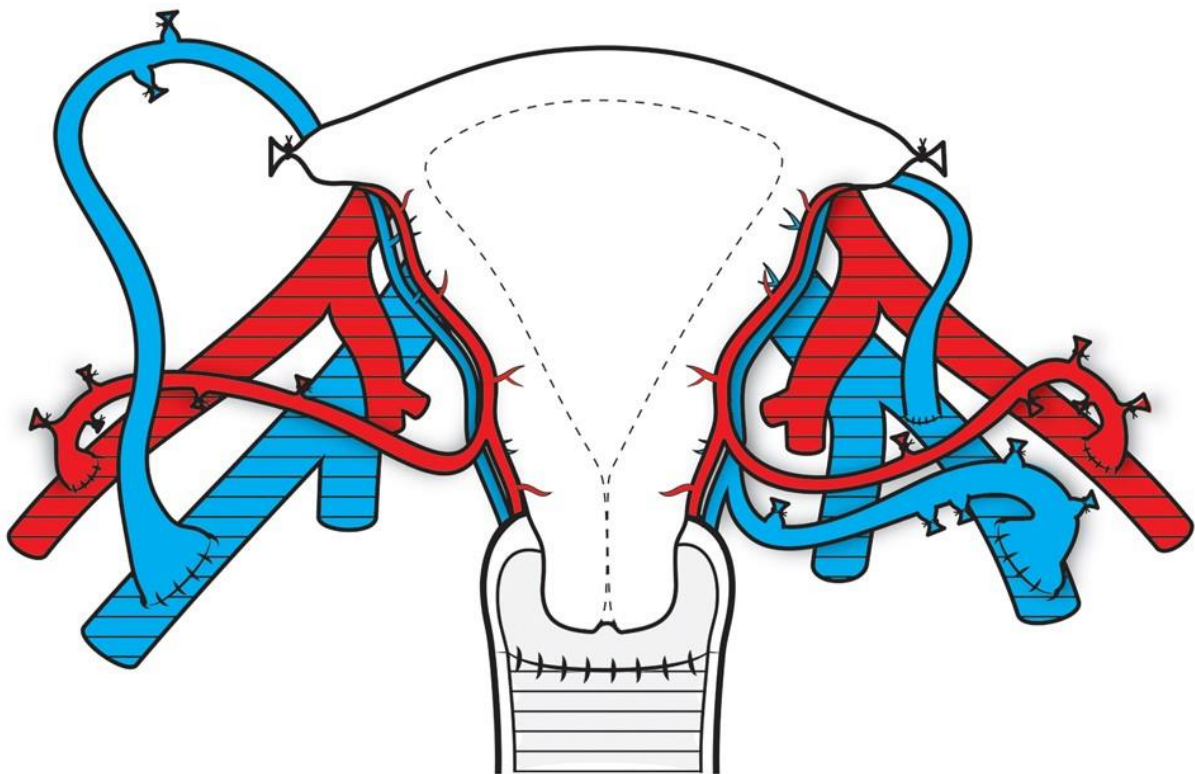


Fig 1 depicts a schematic illustration of the vascular and vaginal anastomoses in the recipient. The anterior segments of the internal iliac arteries are anastomosed in an end-to-side manner with the external iliac arteries bilaterally. The deep uterine vein and the uterine branch of the utero-ovarian vein are anastomosed end-to-side to the external iliac vein, located on the left side of the recipient. The utero-ovarian vein is anastomosed end-to-side with the external iliac vein, located on the right side of the recipient. Adapted from Brännström M, et al. 2023.

It is crucial to understand that a transplanted uterus does not facilitate natural reproduction; rather, it is utilised alongside in vitro fertilisation (IVF) procedures performed externally on the recipient's body. Besides, the transplant is designed to be a temporary measure, with recipients expected to undergo a hysterectomy after achieving one or two successful pregnancies. This approach is adopted to eliminate the necessity for a lifelong intake of immunosuppressive drugs, which carries an associated higher risk of infection.

Like other organ transplant procedures, uterine transplantation necessitates clearances at multiple levels. Encouragingly, the cost associated with these procedures is decreasing, as patients are now typically discharged on the 14th day following the transplant.

The initial UTx attempt took place in Saudi Arabia in 2000, which regrettably failed due to the necrosis of the transplanted uterus. However, subsequent successes emerged in Sweden in 2014, with the first live birth resulting from UTx. Numerous countries, including Brazil, China, the Czech Republic, Germany, India, Serbia, Turkey, and the United States, have made breakthroughs in UTx since then. Notably, there have been 71 uterus transplants and 55 infants born as a result of these treatments as of today (Table 1). Twelve of these children were born after obtaining a cadaveric uterus.

Table 1: Status of uterus transplantation worldwide

Cases	From year	Type of case	# cases	# Surgical successes	# LD cases	# LD post-op complications
Saudi Arabia	2000	Laparotomy LD	1	0 (0%)	1	0 (0%)
Sweden	2012	Laparotomy LD	9	7 (78%)	9	1 (11%)
Turkey	2011	DD	1	1 (100%)	n/a	n/a
China	2015	Robotic LD	1	1 (100%)	1	0 (0%)

Cases	From year	Type of case	# cases	# Surgical successes	# LD cases	# LD post-op complications
USA (Cleveland)	2016	DD	8	6 (75%)	n/a	n/a
Czech Republic	2016	Laparotomy LD	5	4 (80%)	5	2 (40%)
		DD	5	3 (60%)	n/a	n/a
USA (Dallas)	2016	Laparotomy LD	13	8 (62%)	13	2 (15%)
		Robotic LD	5	5 (100%)	5	2 (40%)
		DD	2	1 (50%)	n/a	n/a
Brazil (Sao Paulo)	2016	DD	1	1 (100%)	n/a	n/a
Germany	2016	Laparotomy LD	4	4 (100%)	4	0 (0%)
India	2017	Laparoscopy LD	4	4 (100%)	4	0 (0%)
Lebanon	2018	Laparotomy LD	1	1 (100%)	1	0 (0%)
France	2019	Robotic LD	1	1 (100%)	1	1 (100%)
Spain	2020	Robotic LD	1	1 (100%)	1	0 (0%)
Brazil (Barretos)	2021	Robotic LD	1	1 (100%)	1	0 (0%)

*LD, live donor; DD, deceased donor. Adapted from Brännström M., et al. 2023.

India initiated its UTx journey in 2017 when Galaxy Care Hospital in Pune (Figure 2) conducted the country's first two UTx procedures. The pioneering recipient was a 21-year-old woman born without a uterus (Mayer-Rokitansky-Küster-Hauser syndrome) who gave birth to the first Indian UTx-born baby, Radha, on October 18, 2018, weighing 1.45 kg and delivered at 31 weeks of gestation due to preterm labour. Radha is now five years old and healthy. The second recipient was a 24-year-old woman with uterine scarring due to multiple abortions and stillbirths. She delivered on May 24, 2019, at Pune's Ruby Hall Clinic, weighing 1.2 kg and born at 28 weeks of gestation due to intrauterine growth restriction. This baby boy is now four years old and thriving. Both received uteri from their mothers as living donors.

These groundbreaking achievements have firmly placed India on the UTx research and practice map, offering new avenues for women with AUI to fulfil their aspirations of motherhood. Nonetheless, several hurdles and obstacles must be surmounted before UTx can become a widely accessible option for Indian women.

One significant challenge pertains to the lack of awareness and education about UTx among both the general public and the medical community. Many women with AUI remain unaware of the potential of UTx or are hesitant to seek assistance due to social stigma and cultural constraints. Similarly, numerous healthcare professionals are unfamiliar with the indications, criteria, protocols, and outcomes of UTx or harbour scepticism regarding its safety and effectiveness. Consequently, there is a pressing need for increased dissemination of UTx information and evidence through various media channels and professional platforms.



Fig 2: My team addressing the press conference following the first uterus transplantation in India in 2017. Photo credit: Indian Express

Another challenge lies in the scarcity of UTx donors and recipients in India. Unlike other organ transplants that save lives, UTx is a procedure that enhances quality of life but is fraught with ethical and emotional complexities for all parties involved. Identifying suitable donors willing to altruistically contribute their uteri is a formidable task, particularly in a country with low organ donation rates. Additionally, identifying eligible recipients who meet UTx's strict criteria is challenging, given that many women with AUFI may have other medical or psychological contraindications that preclude them from undergoing UTx.

The high cost and limited availability of UTx in India pose a third significant challenge. UTx is a costly procedure, requiring specialised infrastructure, equipment, personnel, and medications. The estimated cost of UTx in India ranges from Rs 11 lakh to Rs 15 lakh per case, placing it beyond the financial reach of most Indian women grappling with AUFI. In addition, there are only a handful of specialised centres in urban areas with the requisite expertise and experience to perform UTx. Consequently, additional financial support from both the government and private sectors is necessary to render UTx more affordable and accessible to Indian women.

A fourth challenge emerges from the lack of standardised guidelines and regulations governing UTx in India. UTx remains an experimental and evolving procedure, necessitating rigorous monitoring and evaluation of its short-term and long-term outcomes. Regrettably, India lacks a uniform protocol or policy for UTx that outlines the indications, criteria, procedures, follow-up measures, reporting mechanisms, and auditing processes for UTx cases. Moreover, a national UTx registry or database in India is conspicuously absent, resulting in the absence of comprehensive data collection and analysis pertaining to UTx cases. Hence, it is imperative for stakeholders in India's UTx landscape to foster collaboration and coordination, establishing a common framework that ensures quality, safety, and accountability in UTx.

Importantly, ethical considerations have sparked debates regarding the justification of uterus transplants. This debate encompasses extensive literature addressing the psychological and physical risks as well as complications associated with immunosuppressive therapy. Concerns have been raised regarding the well-being of living donors, who may potentially regret their decision to donate. Living donation should only proceed after obtaining informed consent from the donor and following comprehensive counselling by medical professionals and psychologists. I would like to highlight that over the past two years, we have performed eight transplants while keeping several others on hold. This cautious approach is being taken to ensure that couples and their family members are entirely certain and committed to the transplant procedure.

However, amidst these challenges lie numerous opportunities and prospects for UTx in India. India possesses a substantial pool of potential donors and recipients for UTx, coupled with a rich tradition of medical and surgical innovation and excellence. India's culturally

diverse society highly values motherhood and family, while also respecting women's autonomy and dignity. This favourable backdrop fosters significant potential for UTx to become a viable and invaluable choice for Indian women grappling with AUI who aspire to experience the joys of pregnancy and childbirth.

Furthermore, guidelines for UTx should underscore the paramount importance of safeguarding the rights and well-being of children born through the procedure, ensuring comprehensive cost agreements between patients and practitioners, and strictly prohibiting any mediation involving commercial uterus provision. Compliance with legal, ethical, and medical society guidelines, with the endorsement of the implementation facility's ethics committee, is essential in clinical UTx studies. Adequate surgical techniques are to be honed through essential animal experimentation, including non-human primates, recognising the multidisciplinary nature of the procedure. It is imperative to assemble a diverse medical team encompassing a wide range of professionals. Achieving social consensus on the clinical application of UTx mandates continuous research, information dissemination, and opinion gathering.

Currently, developments in uterus transplantation encompass robotics, aiming to reduce surgical duration, enhance precision, and minimise blood loss. A non-invasive rejection diagnosis is being explored to identify rejection biomarkers in body fluids, replacing the need for cervical biopsies. Expanding the donor pool involves considering altruistic living donors and potentially female-to-male transgender hysterectomy cases. Reusing a transplanted uterus after a planned hysterectomy may also be an option. To further broaden donor criteria, accepting donors beyond the age of 55 is being explored. Bioengineering the uterus involves using patient-specific scaffolds and stem cells to overcome organ shortages, though human trials may still be a decade away.

As a uterine transplant surgeon, I have had the privilege of witnessing firsthand the transformative impact of UTx on the lives of women with AUI and their families. I have also observed the challenges and hardships they face before, during, and after UTx. I firmly believe that UTx transcends being a mere surgical procedure; it represents a social movement that empowers women with AUI to reclaim their reproductive rights and roles.

I implore my colleagues in the transplant medical field to unite in this movement. Let us work diligently to expand our knowledge about UTx, share our experiences and expertise, conduct further research and trials, advocate for increased resources and support, and provide comprehensive and compassionate care to women with AUI opting for UTx.

In conclusion, uterine transplantation represents a remarkable journey of hope and perseverance. Our collective efforts have brought us to a juncture where we can offer a new lease of life to women facing uterine factor infertility. In this discipline, however, we must continue to pursue excellence, innovation, and equity. As we continue our journey in the

field of uterine transplantation, may the words of Sir William Osler serve as motivation: "The good physician treats the disease; the great physician treats the patient who has the disease." In uterine transplantation, we do more than treat a medical condition; we restore hope, aspirations, and the joy of motherhood.

Thank you for your unwavering commitment to the field of transplantation, and I look forward to witnessing India's uterine transplantation's sustained progress and success.

With warm regards,

Dr. Shailesh Puntambekar,
Uterine Transplant Surgeon.

The Emerging Role of Robots in Renal Transplant Surgery



Dr. (Prof) Anup Kumar (Picture), Dr. Sumit Aggarwal

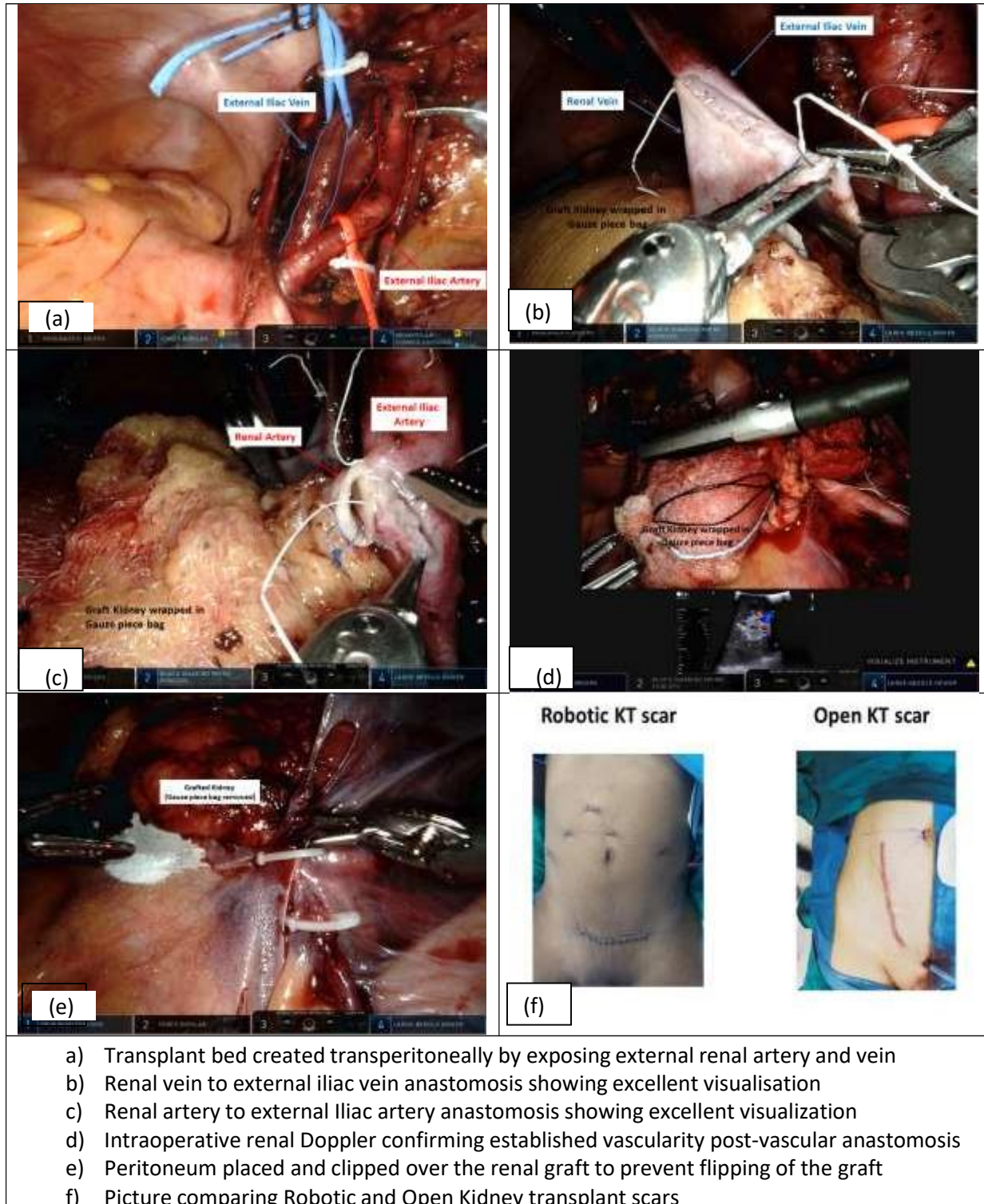
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Robot-assisted kidney transplant (RAKT) has emerged as a groundbreaking advancement in the field of transplantation surgery. The first full RAKT was reported in a morbidly obese patient by Giulianotti *et al.* (1) from Chicago in 2010. RAKT combines the precision of robotic systems (DaVinci, Intuitive Surgical, Sunnyvale, CA, USA) with the expertise of skilled surgeons to enhance the overall procedure.

Unlike traditional open renal transplant surgery, RAKT utilises minimally invasive techniques, resulting in smaller incisions, reduced blood loss, lesser post-operative pain, and quicker recovery times for patients. The enhanced visualisation with high-definition 3D imaging provides a magnified view of the surgical site, and the robot's articulated arms provide unparalleled dexterity and remarkable precision, ultimately leading to improved graft placement and vascular anastomosis.

RAKT also improves access to renal transplants in obese patients and has low wound complication rates (3.8%) in obese individuals. (2) A recent study from India with a median follow-up of 5 years has shown that RAKT outcomes are non-inferior to open transplant. (3) Technical modifications, experience, and expertise would further improve the RAKT's overall outcomes.

The learning curve for RAKT is short, which is easily achievable (4), and surgeons already performing renal transplants and robotic surgeries will be able to learn even faster. With the increasing number of transplant and robotic centres in India, RAKT would be increasing in number and would also act as a testament to the remarkable strides in surgical innovation.



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Women in Transplantation

Female Nephrologists: Their Legacy, Current Struggles, and the Way Forward



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With more women joining the nephrology workforce in recent years, the challenges faced by them are being appreciated more and more. The advent of women nephrologists has been a significant catalyst for progress in the realm of medical science and nephrology. This phenomenon of societal change in attitude and acceptance happened more than a hundred years ago, when India had the privilege of having its first woman physician, Dr. Anandi Gopal Joshi. The contribution of women scientists in renal physiology such as Phyllis Adele Bott and Margaret Mylle has been acknowledged over the years.

The major push for women physicians in our sub-speciality happened half a century ago, when Prof. Priscilla Kincaid-Smith had the distinction of leading the International Society of Nephrology (ISN) as the organisation's first female president (1972–1975). In India, the first lady nephrologist, Prof. Vidya Acharya, was one of the pioneers in Indian nephrology. She was instrumental in starting the first nephrology services in western India, one of the earliest in India. Her inspiring life has, over the years, transformed the professional landscape for lady nephrologists.

On a global scale, as well as in India, there is an increasing representation of women in the medical profession, including nephrology. Despite progress, there are still challenges and barriers that often discourage female physicians from considering nephrology as a profession. One of the areas where women nephrologists are shying away is in the field of transplantation. Long, unpredictable hours and the overall stress often make them think twice before committing wholeheartedly to transplantation. Not only physicians but even transplant surgeons often have to make major sacrifices.

To address this issue and help women surgeons and physicians take up transplantation as a specialty, there is a strong need for professional bodies to come forward and deliberate as to how to make things easier for women. The first step is to look at issues of gender equity. Gender prejudices include inadequate acknowledgement, pay inequity, and insufficient representation in national and international societies. They often face stereotypes and prejudices that hinder their professional growth. Notably, the issue of pay equity remains a pronounced challenge, specifically within the private sector pertaining to female clinicians.

For young professionals, balancing a demanding career in transplantation with personal responsibilities can also be overwhelming. Societal expectations and cultural norms impose limitations on women pursuing careers in this difficult subspecialty of transplantation. Objective evaluation and concrete steps in addressing these issues will go a long way in increasing the involvement of young women in transplantation.

Resident's Corner

Socio-Economic Challenges and Renal Transplantation in West Bengal: A Resident's Experience



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Chronic kidney disease (CKD), with its increasing prevalence, affects almost all sections of our community. Apart from the clinical morbidity and mortality risks it imparts, there are certain challenges faced by CKD patients that are exclusive to their socio-economic niches. Renal transplantation remains the epitome of care offered to end-stage kidney disease (ESKD) patients, which can not only transform the lives of the patient but also positively impact the lives of the carers and family members.

According to the studies conducted in India, 42.7% of the CKD patients have a monthly income of less than 5000 rupees. With a total of 64.13% of the rural population, the prevalence of CKD in the rural population is on the rise. The hospital where I am currently training serves such populations maximally, which has given me an opportunity to study firsthand the challenges faced by the ESKD patients as well as by the treating nephrologists; rather, the treating transplant team would be a better choice of word here.

Keeping the clinical aspects of transplantation aside, our patients face challenges in terms of lack of economic stability, lack of access to a proper health care system, poor education and awareness, malnutrition, poor housing, gender disparities, carer fatigue, psychological trauma of feeling like a burden, loss of financial independence, and loss of employment resources. All of these are intertwined in origin and feed each other. The availability of a healthy donor often remains a challenge. In cases of live donors, there is conspicuous gender discrimination due to the prevailing notion of males being the earning members. With the questionable ethics and legality of incentive-based donors, cadaveric donation needs to be strengthened to fulfil the unmet need.

Over the last few years (barring the COVID-19 hit years), increasing awareness and organ donation drives have resulted in higher numbers of deceased donor transplantation in our country (for kidneys, from 542 in 2013 to 1541 in 2022); however, with a total of 25 deceased-donor renal transplants out of the total 1048 (263 live-related and 785 live-unrelated) renal transplants in West Bengal, our state has a very long way to go. Lack of a proper recipient list that is updated from time to time according to the age, sensitization of the patient, and other parameters remains a hindrance.

Transplant patients in their early years need scrutiny and frequent investigations, including drug level monitoring. Even if the tests and doctors' consultations are free in most public sectors, their transport and the daily wage loss of the accompanying person incur a lot of out-of-pocket expenditure, and poor follow-up causes disruption of the free medicine supply, leading to an inevitable noncompliance and a poor outcome.

To implement the distributive justice incorporated in the slogan HEALTH FOR ALL, the support system should consider the occupational and psychosocial rehabilitation of the recipient, which can be initiated by their own village panchayat administrations. The emphasis should be on skill development for economic sustainability and foremost on generating a sense of self-reliance rather than a state of financial dependency. Awareness regarding these aspects, including the pharmaco-economics of transplantation, amongst health care workers is necessary for improving the quality of life of our transplant patients.

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Revolutionizing Healthcare: The Role of Artificial Intelligence in Transplantation



Dr. Himanshu Verma (Picture), Dr. Sourabh Sharma

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In the ever-evolving landscape of healthcare, artificial intelligence (AI) is emerging as a game-changer, and one of its most promising frontiers is in the field of transplantation. The fusion of cutting-edge technology with the critical need for organ transplants has the potential to save countless lives and streamline the transplantation process like never before.

AI's impact on transplantation is multifaceted, offering solutions at every stage of the journey, from donor identification to post-transplant care. Here is a glimpse into how AI is transforming the world of transplantation:

Organ Matching Precision: AI algorithms are revolutionising organ matching by considering a broader range of factors, including genetic compatibility, recipient health, and geographical proximity. This precise matching reduces the risk of organ rejection and enhances transplant success rates.

Predictive Analytics: AI can predict the availability of organs for transplant by analysing health data trends and organ procurement information. This proactive approach helps medical teams prepare for surgeries and improves the chances of finding suitable donors.

Surgical Precision: During transplantation surgeries, AI-assisted robotic systems enhance the precision and control of surgeons, reducing the risk of complications and shortening recovery times for patients.

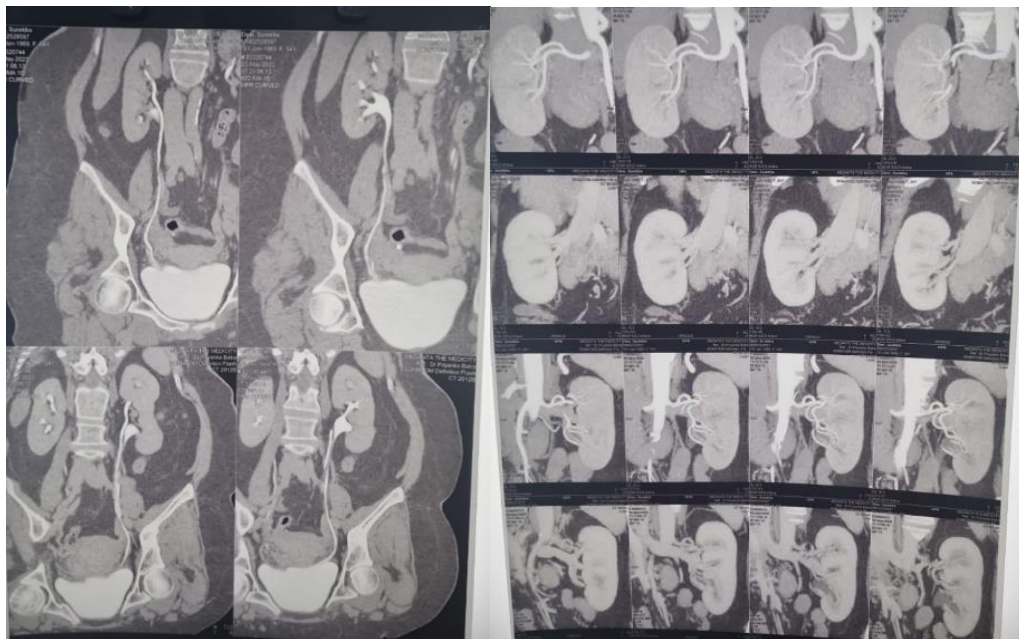
Post-Transplant Care: AI-powered monitoring tools enable real-time tracking of a recipient's health post-transplant. Any deviations from expected parameters can trigger early interventions, ensuring better postoperative care and patient outcomes.

Data Analysis: AI can process vast amounts of medical data to identify patterns and develop predictive models for transplant outcomes. This data-driven approach aids in the continuous improvement of transplantation procedures.

Ethical Considerations: The use of AI in transplantation raises ethical questions about data privacy, algorithm bias, and decision-making transparency. It is essential to address these concerns to maintain trust in the system.

As AI continues to evolve, its role in transplantation will expand further, offering hope to patients on transplant waiting lists and improving the quality of life for transplant recipients. However, it is crucial to strike a balance between technological advancements and ethical considerations to ensure that AI serves as a reliable and ethical ally in the quest to save lives through transplantation.

Quiz of the month



Picture credit- Dr Jitender Kumar, Dr Saurabh Joshi, Accord Hospital, Faridabad, Haryana.

This is a CT angiogram of a 48-year-old male donor who has volunteered to donate his kidney to his 55-year-old brother. What conclusions can be drawn from these images, and what key precautions should be considered for this donor?

Upcoming Conferences

**39th Annual Conference of Indian Society of Nephrology,
West Zone 2023**

January 5-7, 2024

Rajkot

The 5th Kolkata Transplant Colloquium

January 12-14, 2024

Thimphu, Bhutan

ISNSCCON 2024

February 8-11, 2024

Hyderabad, India

**Mayo Clinic Nephrology, Hypertension and Kidney Transplantation Update for the
Clinician 2024**

February 16-18, 2024

Coronado, California, USA

ISN World Congress of Nephrology

April 13-16, 2024

Buenos Aires, Argentina

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Members of ISOT are invited to submit articles, personal perspectives, and stories related to the field, which may include intriguing cases, appealing images, jokes, and cartoons, as well as news regarding regional and state meetings. The maximum length for submissions is between 800 and 1,000 words. Please include a statement stating that your entry does not violate any copyrights. Kindly submit to isotnewsletter@gmail.com

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