RESEARCH ORIGINAL ARTICLE

The Jordanian Kidney Transplant Experience: A Glorious Past and A Challenging Present

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ABSTRACT

Jordan was one of the first Arab countries to enact legislation governing organ donation and transplantation. Since that time, Jordan has seen an increase in the frequency of kidney transplants performed utilizing organs from living donors. Jordan has been a reputable regional center for kidney transplantation and has a long history of excellence in the field.

Jordan has a low rate of kidney transplants from deceased donors despite its legality in the Jordanian legislation, as well as the availability of highly skilled nephrologists and transplant surgeons and advanced health care. This is quite alarming and could be caused by a number of different factors. The absence of a formal government plan to control brain death donation is the most important factor.

The goals of this study are to provide a description of the current state of kidney transplantation in Jordan, a summary of the most significant barriers to expanding kidney transplantation efforts that focus on kidneys donated by deceased donors, and suggestions for increasing the number of kidney transplants from brain-dead donors.

KEYWORDS - kidney transplant, kidney paired exchange, end stage renal disease, kidney donation

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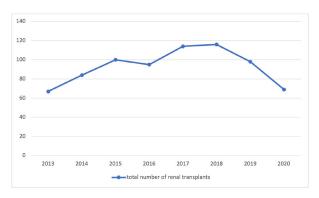
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INTRODUCTION

Kidney transplantation (KT) remains the gold standard renal replacement therapy(1), as it not only corrects renal functional impairment but also provides an excellent and near-normal quality of life for recipients. Additionally, it is the most cost-effective therapy. (2)(3)(4).

Jordan performed the first kidney transplant from a living donor in 1972 (5). This had never been performed before in the Middle East. In 1977, the Jordanian parliament passed legislation regulating organ donation and transplantation, making the country one of the first in the Arab world to regulate these practices (6). Because of these advancements, Jordan has witnessed a rise in the number of kidney transplants that are performed using organs from living donors. Jordan has traditionally had an excellent reputation in the medical field and has served as a well-respected regional center for kidney transplantation since the late 1990s, servicing patients from the Arab Gulf region and around the Middle East. The number of transplant surgeries performed in Jordan, increased from 185 in 2004 to 238 in 2017, only to fall to 102 in 2020 as a result of Covid-19 (7).

Figure 1. Total Number of Kidney Transplants Performed in Jordan between 2013 and 2020 for Jordanian Recipients



However, the percentage of transplants performed using organs from brain-dead donors remains extremely low, and the number of such procedures performed each year typically does not exceed 1 to 2 cases. This low frequency of kidney transplants from deceased donors in Jordan, despite its legality, the availability of well-trained transplant surgeons and nephrologists, and advanced medical facilities, is quite concerning and could be attributable to a variety of reasons. The most significant factor is the lack of a structured governmental strategy to regulate the process of brain death donation. Although Islam, which supports organ donation, is practiced by the majority of Jordan's population,

there is still a substantial shortfall in the number of organ donors after brain death.

This study's objectives are to provide a description of the current state of kidney transplantation in Jordan; to provide a summary of the most significant obstacles that stand in the way of expanding kidney transplantation efforts that concentrate on kidneys donated by deceased donors; and to suggest solutions to increase the number of kidney transplantation from the brain dead donors.

METHODS

DATA COLLECTION - Data on ESRD status in Jordan was obtained by utilizing two primary databases: the National Registry of End Stage Renal Disease, provided by the Ministry of Health in Jordan, and the database of the Jordanian Center for Organ Transplantation Directorate. The National Registry of End Stage Renal Disease provided comprehensive information on the prevalence, incidence, and related statistics of ESRD in Jordan. This database served as a valuable source for understanding the overall landscape of ESRD in the country. Additionally, the database of the Jordanian Center for Organ Transplantation Directorate was utilized to gather data specifically related to renal transplants. This database contained records of patients who underwent renal transplantation in Jordan during the period from January 1, 2013, to March 30, 2021. The combination of these two databases allowed for a comprehensive collection of data regarding ESRD and renal transplantation in Jordan, providing a robust foundation for the study.

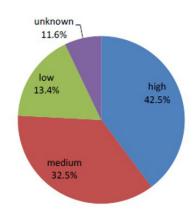
LITERATURE REVIEW - To supplement the collected data, a thorough review of existing literature on renal transplantation and ESRD in Jordan and worldwide was conducted. Articles published in reputable scholarly sources, including PubMed and other search engines, were analyzed. The literature review provided additional insights into the current knowledge, trends, and challenges related to renal transplantation and ESRD, and contributed to the contextualization of the study.

DATA ANALYSIS - Since this article is purely descriptive, no specific data analysis was conducted. The focus was on presenting and summarizing the gathered data in a clear and concise manner to provide an overview of ESRD status and renal transplantation in Jordan.

ESRD AND CANDIDACY FOR TRANSPLANTATION

According to the 12th Annual Report of the National Registry of ESRD published by the Ministry of Health in 2019 (8), the number of patients treated at dialysis units was 6,316, with male patients comprising 61% of the total number (a male-to-female ratio of 1.5:1). In 2019, there were 750 new cases of ESRD, and approximately two patients were added to the transplant waiting list daily. Jordan documented an overall incidence rate of 98 cases per million population with a prevalence rate of 864.5 cases per million, which is more than double the prevalence of pooled prevalence among Middle Eastern countries, which was found to be 360 per million population (9,10). However, it is significantly lower than the prevalence rate reported in the USA, which was found to be 2,200 per million population (11). But with the significantly lower number of transplants done, the problem of ESRD may exacerbate in the future (9,10). In Jordan, 42.5% of the 2,598 patients deemed as candidates for transplantation in 2020 were deemed high priority (figure 2).

Figure 2. Distribution of End-Stage Renal Disease Patients Eligible for Kidney Transplantation by Priority Level



Dialysis became accessible in Jordan in 1968. Since then, dialysis centers have steadily expanded in terms of geographic coverage and capacity (12). The country's economic prosperity has contributed to the development of services across the country. Jordan University Hospital established the country's first renal dialysis facility in 1981. The equipment was a portable REDY "Sorbs system" that could be transferred between hospitals. Currently, there are 87 operational dialysis units throughout the country. The private sector manages 36 units (41%), Royal Medical Services (RMS) manages 12 units (14%), and university hospitals (Jordan University Hos-

pital and King Abdullah University Hospital) manage two units. The total number of dialysis machines (932) is distributed as follows across each unit: 435 (46.7%) machines in MOH units, 379 (40%) machines in private sector hospitals, 84 (9%) machines in RMS, and 34 (3%) machines in university institutions (8).

Unfortunately, Jordan's transplant community faces major difficulties, such as organ shortages and long wait times on national waiting lists. In Jordan, 2,598 (35.6%) of ESRD patients were transplant candidates, 4,321 (59.3%) were not, and 371 (5.1%) lacked data (11). The primary reasons for patients' ineligibility for transplantation were as follows: advanced age, which accounted for 1,766 patients (49.8%); medical reasons, which accounted for 1,188 patients (33.5%); malignancies, which accounted for 60 patients (1.7%); and unknown causes, which accounted for 212 patients (6%) (8).

Despite the fact that the government covers the cost of dialysis for all Jordanians diagnosed with ESRD, the 2019 data showed that 98% of patients were insured by one of the various types of health insurance (8). However, there are still costs for the patient and family due to being unable to work full-time, as well as the costs of transportation and other non-directly related comorbidities.

LIVING DONOR KIDNEY VS DECEASED DONOR KIDNEY TRANSPLANTATION

Living donor kidney transplants have significantly better outcomes, a better prognosis, and a decreased susceptibility to rejection than deceased donor kidney transplants (1)(13)(14). However, deceased donors are the primary source of KT worldwide. In Jordan, however, the situation is considerably different: the primary source of organ donation for KT is from living donors, whereas the shortage primarily stems from deceased kidney donors. Unfortunately, only two of the 100 kidney transplants performed in 2020 came from brain-dead donors, even though more than 800 new ESRD patients started on hemodialysis that same year. Between 2013 and 2021, a total of 815 kidney transplants were performed in Jordan. Only 8 of those transplants, however, came from brain-dead donors (Jordanian Centre for Organ Transplantation Directorate 2013-2021) (8)(12). Jordanian regulations limit living organ donations to close family members only, up to the fifth related degree, thus limiting the possibilities available to ESRD patients by forbidding friends, neighbors, and altruistic donors from being included to broaden the candidates'

options. The regulations on donation after brain death, drafted in 1984, were the first legal documents in both Jordan and the Middle East to address the concept of donation after brain death. Donation after brain death (DBD) is the only type of deceased donation utilized in Jordan. Given that the DBD source has not been properly tapped into, there is likely to be strong opposition to enlarging the pool to include donations after cardiac death (DCD). However, this warrants additional consideration.

The shortage of compatible living donors can be alleviated in part by broadening the pool of potential donors. This could involve accepting kidneys from relatives beyond the fifth degree, and potentially expanding the options to include neighbors and friends, subject to strict regulations and thorough social work investigations. However, the scarcity of organs from deceased donors can be largely addressed by initiating an organ donation after brain death program and by establishing a national center for organ donation and transplantation. This approach is consistent with the majority of countries that have active deceased donor organ donation programs, and such a center would serve as the primary regulatory body for all organ transplantation activities in Jordan.

GENDER DISPARITIES IN KIDNEY DONATIONS

According to the data records from the Jordanian Center for Organ Transplantation Directorate (2013-2020), women in Jordan donated 45% of all kidneys, despite receiving only 29% of all donated kidneys (figures 3,4). Men constitute around 60% of all ESRD patients, while women constitute the remaining 40%. Combining these observations, it becomes clear that women donate more kidneys than men relative to their disease burden. This disparity can be attributed to women possessing a more favorable attitude and a deeper understanding of the significance of organ donation, even though they have comparable basic knowledge about organ donation as men (15).

This disparity underscores the generous and selfless acts of women in our society. They have demonstrated immense compassion by donating their kidneys to save lives. This contribution merits acknowledgment and should inspire further promotion of organ donation. Numerous studies from the US, India, and Canada have indicated that men are more likely to receive a kidney transplant than women (16). Similarly, global published research shows that women are more likely to donate a kidney than men (17).

Figure 3. Distribution of Renal Transplants performed for Jordanians in Jordan during 2013-2020 according to living donor sex

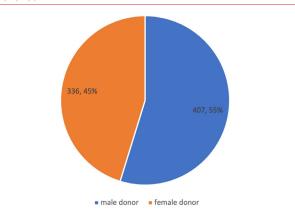
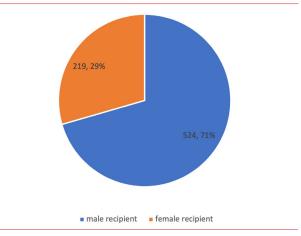


Figure 4. Distribution of Renal Transplants performed for Jordanians in Jordan during 2013-2020 according to recipient sex



One potential explanation for the observed trend of females donating more organs but receiving fewer transplants concerns immunological factors associated with family connections. Mothers, especially, might encounter difficulties in receiving organs from their children or spouses due to past exposures during pregnancy or childbirth. Such exposures can lead to the production of antibodies against specific antigens, heightening the risk of rejection when receiving a kidney from close family members. This immunological incompatibility narrows the pool of potential donors for mothers, complicating the quest for an ideal match. This dynamic poses heightened hurdles for females with ESRD in Jordan, where donors must be within a fifth-degree connection or closer (18).

CHALLENGES

PROGRESS IN DECEASED DONORS PROGRAM

- The goal of any nation's transplant community is to establish a deceased donor program robust

enough to provide organs for every patient on its waiting list. However, the challenges of setting up a deceased donor KT program starkly differ from those of a living donor KT. Successfully rolling out deceased donor KT requires a system that integrates communication with sectors outside the immediate realm of transplantation (like neurosciences, forensic medicine, the legal system, government and non-government organizations, and the public). This also calls for coordination with multiple healthcare providers who operate with differing priorities.

To establish an organ donation after brain death program in Jordan, it's imperative to have more than the existing infrastructure; there must also be strong support from the authorities. While the country might possess the necessary healthcare facilities and skilled professionals, the absence of robust support from the government presents a formidable challenge. Lacking a firm commitment from the state, resource allocation, effective policy implementation, and fostering the needed shifts to promote organ donation after brain death become problematic. Moreover, fostering close collaboration between healthcare institutions, government bodies, and religious leaders is vital. This alliance can address potential religious apprehensions and ensure the program's cultural acceptance.

Establishing an organ transplantation center in Jordan is essential to act as an umbrella for all organ transplantation endeavors. This center would offer a unified and coordinated method for organ donation, recovery, transplantation, and subsequent care and observation. It would simplify procedures, ensuring effective organ distribution, thorough recipient evaluation, and timely transplant activities. Moreover, a national organ transplantation center would promote collaboration among diverse healthcare professionals, transplant surgeons, and auxiliary staff, championing a multidisciplinary approach to organ transplantation. By consolidating knowledge and resources, the center would elevate the caliber of transplantation procedures and patient results. It would also hold a pivotal position in bolstering awareness, enlightening the general public and the medical community, and fostering a conducive organ donation environment in Jordan. By laying this foundation, the center would not merely address current challenges but also lay the groundwork for a thriving and enduring organ transplantation initiative in Jordan.

RELIGIOUS ACCEPTANCE - Religious perspectives profoundly influence individual perceptions of organ donation. Certain religious communities might deem the ethical aspects of organ donation

and issues surrounding brain death as controversial. These reservations can induce hesitancy and opposition among potential donors and their kin, potentially diminishing the number of organ donors after brain death (15).

The impact of religious beliefs was once thought to be one of the biggest obstacles to organ donation in Jordan following brain death. however, Recent research has shown that small percentage of the population are reluctant to contribute owing to religious considerations. The study in question, however, did not distinguish between organ donation while a person is still alive versus donation after brain dead. (19).

We believe that religious opposition to the topic of organ donation began when in the early 1970s, some religious leaders voiced concerns and mistrust regarding organ donation after brain death due to their unfamiliarity with the medical procedures involved. These theological convictions have, however, significantly changed throughout time. Due to developments in medical knowledge, particularly a better understanding of brain death, religious authorities in Jordan and other Islamic nations have mainly acknowledged and embraced the compatibility of organ donation with religious precepts. Organ donation after brain death has been made clear by numerous religious authorities and academics, who also claim that it is permissible and even considered a very honorable and compassionate act (20).

It is crucial to note that Islam, as the predominant religion in the country, strongly supports and promotes organ donation. Compassion, saving lives, and helping people in need are qualities that are heavily emphasized in Islamic teachings(21). The permissibility of organ donation after brain death has been upheld by a number of significant Islamic scholars who have issued fatwas (religious rulings), describing it as a generous act and an extension of preserving life (21).

To overcome these religious challenges, continuous efforts are essential to enhance awareness, engage religious leaders, and emphasize the ethical and life-preserving advantages of organ donation. We strongly believe that establishing of an organ transplant center in Jordan would be instrumental in navigating this issue. By addressing these difficulties and encouraging discussion, we could potentially be able to increase acceptance and interest in organ donation after brain death in Jordan.

SOCIAL ACCEPTANCE - The low volume of deceased donor KT in Jordan can be attributed to lack of public awareness about the importance

of KT and an underestimation of the physical and mental health burden of ESRD on patients.

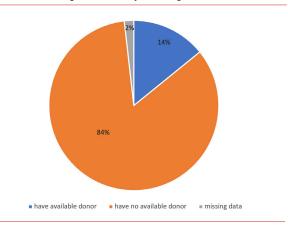
A study conducted in Jordan to evaluate knowledge and attitudes toward organ donation utilized 15 qualitative interviews and 500 quantitative surveys between November 2018 to April 2019. It was discovered that only 49 (9.8%) had registered to donate organs. Barriers to donation included a lack of trust in the healthcare system and a sense of lack of autonomy. Specifically, 39.3% felt that donors should dictate the recipients of their organs, and many expressed reluctance to donate to individuals with alcoholic liver disease or criminal records. The survey indicated that the internet and social media were the primary sources of information about organ donation, while formal education and healthcare providers were among the least referred to. This emphasizes the critical role of online platforms in correcting misconceptions about organ donation and disseminating accurate information (15). Conversely, another study surveying 404 respondents from Jordan indicated that a significant majority (72%) held positive views on organ donation. Supporting findings from the previous study, this research also found that a third of the participants expressed distrust in Jordan's healthcare system concerning organ donation and transplantation (19).

Despite having a positive attitude, the shortage of citizens who have registered for organ donation in Jordan continues to be a major problem. This notion is supported by a recent study that looked at the responses of 1,041 individuals and found that, while an impressive 79.4% of them expressed their support for this noble cause, only 11.9% of them had actually signed up for organ donation. This significant discrepancy begs the question of why most Jordanians support organ donation but are reluctant to register as donors despite having such favorable views. To develop successful tactics for raising organ donor registration rates and eventually saving more lives, it is crucial to delve deeper into this conundrum and examine the underlying variables that lead to this gap (22).

KIDNEY PAIRED EXCHANGE PROGRAM - (KPE) or live donor paired exchange, was created to address the issue of HLA and ABO incompatibility by allowing a living donor to direct the donated organ to a different compatible recipient, with the goal of another donor donating to the first donor's intended recipient(23)(24).

As previously mentioned, Jordanian law forbids organ donation from anybody who is not a fifth-degree relative, leaving a significant number of patients without living donors. The fact that 2,183 patients (84% of patients on the waiting list) are kidney transplant candidates in Jordan and had no accessible living donor (Figure 3)(12), demonstrates the severity of ESRD in the country in the absence of an active deceased donor program. This emphasizes the necessity of developing KPE programs, which may help increase access to KT and, as a result, improve outcomes by enlarging the pool of potential living donors for transplant candidates(25) (26).

Figure 5. Distribution of End-Stage Renal Disease Patients According to Availability of Living Donors in 2020



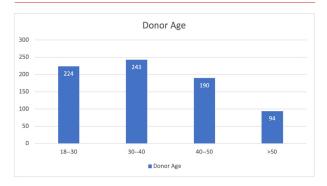
We believe that a well-designed KPE program, which utilizes cutting-edge software algorithm technology and takes into account both international and Jordanian ethics and law, can greatly increase the overall number of kidney transplants. This would bridge the enormous gap between the number of individuals in need of kidney transplants and the total number of ABO and HLA-compatible kidneys available for them, thus decreasing the morbidity and mortality brought on by end-stage kidney renal disease.

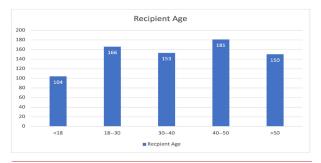
DOCUMENTATION OF OUTCOME - There is a significant lack of comprehensive data on the outcomes of all kidney transplantations (KT) performed in Jordan. This lack of data impedes the evaluation and advancement of transplantation practices in the country.

To address this issue, it is essential to establish a comprehensive registry in Jordan that records and monitors the data and outcomes of KT activities. With the aid of this registry, healthcare providers, researchers, and policymakers will be able to assess the efficacy and safety of various transplantation procedures, immunosuppressive treatments, and post-operative care guidelines.

The World Health Organization (WHO) emphasizes the vital significance of data transparency and documentation in transplantation. The establishment of an open system for tracking

Figure 6. (a) distribution of kidney transplants according to donor age (2013-2020) (b) distribution of kidney transplants according to recipients age (2013-2020)





transplantation outcomes is stressed in Guiding Principle 11 on human cell, tissue, and organ transplantation, which was published by the WHO in 2010(27). This principal highlights that such a system is no longer optional but an essential component of ensuring accountability, quality assurance, and continuous improvement in transplantation practices.

By adhering to the WHO's guiding principle and instituting a robust data registration system, Jordan can contribute actively to global transplantation research and improvement efforts. The availability of detailed data on transplantation outcomes will allow medical professionals working in the field to identify trends, patterns, and areas for improvement. It will promote evidence-based decision-making, the exchange of best practices, and local and worldwide collaborations among transplant services.

Transparent data collection for KT outcomes will also Improve patient safety and care quality. It will allow physicians to identify and address potential challenges, track long-term graft and patient survival rates, and evaluate the efficacy of interventions and medications. This insight will be useful in refining transplantation protocols, improving post-operative treatment measures, and optimizing patient outcomes.

CONCLUSION

Jordan has developed into a significant contributor to the field of KT. However, a pressing challenge remains as the number of organs available for transplantation does not match the increasing number of candidates in need. This underscores the need for continued efforts to establish a donation after brain death program and address barriers to organ donation in the country. Moreover, the establishment of a national transplant center would play a pivotal role in coordinating and regulating all transplant activities, ensuring efficient utilization of resources, and improving patient outcomes. By addressing these challenges and implementing comprehensive strategies, Jordan can further advance its impact in the field of transplantation and provide better access to life-saving organ transplants for its population.

AUTHORS' CONTRIBUTIONS

All authors contributed to manuscript writing and editing.

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