

# Organ Transplantation in Kuwait and the Recent Initiation of a Liver Program

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## INTRODUCTION

Countries with small populations face challenges establishing complex solid organ transplant programs. Liver transplantation requires not only skilled surgeon but also expert anesthesia, perfusionist, intensive care, hepatology, interventional radiology, interventional gastroenterology, pharmacy, immunologists, infectious disease specialist, and expert nursing care. At the same time, it is challenging to attain this extensive setup without a large volume of cases. Moreover, achieving necessary deceased-donor rates is impacted by many factors including the population size. Living-donor transplants offer an alternative; however, initiating a living-donor liver program does not allow room for errors.

## STATUS OF ORGAN TRANSPLANTATION IN KUWAIT

Kuwait has been a local leader in organ transplantation with the first live donor kidney transplant performed in the Arabian Gulf region in February 1979. The Iraqi invasion in 1990 resulted in a major setback, affecting all aspects of life in the country. However, transplant activities recovered quickly with peak volumes in 2004 when 28 deceased and 72 living-related kidney transplants were performed at Hamed Al-Essa center, Kuwait's only transplant center. Since 1993, a total of 1247 kidney transplants have been performed in Kuwait including 437 deceased-donor and 810 living-donor transplants.

The first successful pancreas transplant was performed in 2007, and to date, 6 combined pancreas-kidney transplants in addition to 2 pancreas after kidney transplants have been performed. The demand for more donors is ever present, as the current availability of organs does not meet the demand by far. Since 1993, there have been only 195 deceased donors in Kuwait.

A committee for multiorgan transplantation was established in 2015. This committee met on several occasions and passed major recommendations emphasizing the necessity of deceased-donor liver and heart transplants in the country.

The demand for liver transplants, in particular, is increasing due to the obesity epidemic. Obesity is a major risk factor for nonalcoholic fatty liver disease (NAFLD), a benign entity that may progress to nonalcoholic steatohepatitis (NASH), associated with necrosis, inflammation, hepatocellular injury, potentially leading to fibrosis, cirrhosis, and hepatocellular carcinoma.<sup>1</sup>

The prevalence of NAFLD is estimated to be between 75% and 100% in obese individuals (body mass index > 35 kg/m<sup>2</sup>). NASH, in turn, develops in 30% of patients with NAFLD.<sup>2</sup> The obesity prevalence in Kuwait is estimated to be around 40% in adult male and 50% in adult female individuals.<sup>3</sup> Thus, there is a strong rationale for a liver transplant program in Kuwait that will be prepared to tackle the increasing need.

Liver transplantation is the treatment of choice for patients with end-stage liver disease (ESLD), with 1- and 5-y survival rates of 85% and 68%, respectively.<sup>4</sup> The first liver transplantation for NASH cirrhosis in the United States was performed in 1996 and constituted 0.11% of all liver transplantations performed in the United States that year. By 2007, there had been a 40-fold increase in the number of liver transplantations performed for NASH,<sup>5</sup> and in 2016, NASH became the second leading cause across all patients listed for liver transplantation.<sup>6</sup>

## HEALTHCARE ECONOMICS

Kuwait has a population of 4.25 million, and all Kuwaiti citizens and expats are covered by the healthcare system at no cost. Presently, however, deceased-donor liver transplants are not covered for expats except for first- and second-degree relatives of deceased donors. Expats are covered for deceased-donor kidney and pancreas transplants. Moreover, live donor liver transplants, once implemented, will be covered for both Kuwaitis and expats.

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There are 6 major hospitals in the country with 1 transplant center performing kidney and pancreas transplants. The transplant center is within the same geographical area as another general hospital but represents an independent entity. At each hospital, there is an in-house transplant coordinator to identify potential organ donors and to discuss organ donation with families.

The educational background of transplant coordinators is in nursing, with additional training on how to approach families and how to liaise with local intensive care unit (ICU) teams. The allocation of organs is performed by the local organ donation department.

Before the beginning of liver transplantation in Kuwait, deceased-donor organs have been offered to Saudi centers. In return, many Kuwaiti patients have been placed on the waiting lists in Saudi Arabia and were transplanted mostly with livers from deceased Kuwaiti donors. Kuwaiti patients requiring organ transplantation would also travel abroad with expenses fully covered by the Kuwaiti Government. Most of these patients would undergo their transplant assessment and surgery in the United States or the United Kingdom. A portion of these patients would remain for quite a long time on US or British transplant lists. While waiting, expenses are covered by the Kuwaiti Government, thus representing a massive burden on financial and medical resources. Table 1 shows cost estimates for patients who underwent liver transplantation in the United States, excluding their living expenses and leave-of-absence coverage from their jobs in Kuwait. An additional cost is that of managing liver failure patients in Kuwait without the ability to perform transplants. Indeed, managing ESLD without access to transplant represents a massive burden for ICUs, blood banks, interventional radiology, interventional gastroenterology, and other departments. Lack of a liver transplant program is also associated with insufficient expertise on when to refer patients and thus associated with increased mortality, even among patients able to travel.

### LOBBYING FOR A LIVER TRANSPLANT PROGRAM

Starting a liver transplant program in Kuwait in 2018 posed major challenges. Why would a patient choose to undergo his/her transplant in a new program versus traveling to an established transplant program in a major institution abroad? What would be the consequences if the first operation failed?

Extensive meetings with officials in the ministry of health started in 2015 to obtain approval for the program and to address important questions. All aspects, including costs of the treatment abroad, availability of trained doctors in transplant surgery and transplant hepatology, mortality linked with acute liver failure, costs and burden for managing ESLD, and the crisis to face with increasing relevance of liver failure due to NASH, were discussed. A suggestion was made to collaborate with a highly experienced transplant team to ensure safety and favorable outcomes.

Deficiencies were identified in the following areas: lack of anesthesiologists and intensivists with recent experience in liver transplantation, lack of trained ICU nursing staff, long duration of deceased donor's stay in the ICU, lack of experienced liver perfusionists, and potential inabilities of the blood bank to cope with demands. There was some resistance in starting the program due to concerns that

**TABLE 1.**

**Expenses for 64 Kuwaiti liver transplant recipients in the United States (source: Kuwait Embassy, Washington, DC)**

| Year      | Cost                   |
|-----------|------------------------|
| 2006–2007 | \$3 153 996.55         |
| 2007–2008 | \$8 590 828.62         |
| 2009–2010 | \$7 401 755.80         |
| 2010–2011 | \$8 458 422.86         |
| 2011–2012 | \$16 737 593.45        |
| 2012–2013 | \$5 639 895.78         |
| Total     | <b>\$55 938 782.46</b> |

liver transplants may have a high mortality rate and that the country can afford sending patients for transplantation abroad. As for the country's ability to send patients abroad, we cited the fact that most countries are unable to offer effective deceased-donor transplants with restrictions to transplant nonresidents and that living donation will therefore provide the only alternative. In addition, only a fraction of patients with ESLD are being sent for transplantation based on a lack of expertise. Getting advice from a liver transplant specialist required a long and tedious process of sending patients abroad linked to significant expenses. Consequently, many patients may die from ESLD without ever making it to a transplant list. A major issue was a lack of detailed data on the actual number of patients with ESLD and the associated financial burden. The only data available on financial implications of international liver transplants came from the Kuwait Embassy health office in Washington, which confirmed substantial costs (Table 1).

### INTERNATIONAL COLLABORATIONS

King's College London (KCL) kindly offered their services and agreed to send upon a 24-h notice 2 liver transplant surgeons, a liver anesthetist and intensivist, a perfusionist, and a scrub nurse along with an ICU nurse to Kuwait to join 2 local liver transplant surgeons and 2 local transplant hepatologists. Before the first case, a team from KCL visited Kuwait to tour the facilities with a subsequent reciprocal visit in London when 3 Kuwaiti anesthetists, 2 surgeons, and 1 hepatologist visited KCL for a brief training of 10 d.

### THE FIRST 11 CASES

On January 17, 2018, the first successful liver transplant was performed in Kuwait for a patient with NASH liver cirrhosis. Since then, 10 more liver transplants have been performed. The first 6 liver transplants took place in Mubarak Al Kabeer Hospital, 1 of the 6 general hospitals in Kuwait (2018–2019). Starting in the summer of 2019, the liver transplant service moved to Jaber Al Ahmad Hospital, a newly opened, state of the art megahospital, centrally located in Kuwait. Of the most recent 5 recipients, 2 were awaiting liver transplantation abroad and were brought back to Kuwait as soon as an appropriate donor was available. The increase in transplant activity during the most recent 6 mo reflects the growing trust in the local transplant service with an increase in referrals

**TABLE 2.****Donor/recipient characteristics of liver transplants performed in Kuwait (N = 11)**

|                         |                                                         |
|-------------------------|---------------------------------------------------------|
| Sex (n)                 | Male: 7<br>Female: 4                                    |
| Age (y)                 | Youngest: 33<br>Oldest: 70<br>Median: 56                |
| Recipients demographics | All Kuwaiti                                             |
| Blood group (n)         | Type O: 6<br>Type A: 3<br>Type B: 2                     |
| Diagnosis, n (%)        | NASH: 9 (82%)<br>Alcohol: 1 (9%)<br>Hepatitis C: 1 (9%) |
| MELD-Na                 | Lowest: 16<br>Highest: 31<br>Median: 21                 |
| Donor's age (y)         | Range: 54–24<br>Median: 47                              |
| Donors demographics     | All expatriates                                         |

MELD-Na, model of end-stage liver disease-sodium; NASH, nonalcoholic steatohepatitis.

for transplant consideration and a growing list of patients awaiting transplant. Notably, all donors were expats and all recipients Kuwaitis. Most Kuwaitis are Muslims, and some may not accept brain death as a diagnosis of death.

NASH, as anticipated, was the leading cause of cirrhosis in patients needing transplants (9 out of 11). Additional causes were alcohol-related liver disease and hepatitis C. Only 1 patient had hepatocellular carcinoma. The median model of ESLD-sodium score in our patient population was 21. Table 2 summarizes the characteristics of our 11 transplanted patients.

Currently, 10 out of the 11 recipients are alive with functioning grafts. The only mortality was with the third transplanted patient who had a poor graft function potentially related to donor aspects in the absence of obvious surgical-technical issues.

### FUTURE DIRECTION AND CHALLENGES

Reaching a milestone in the journey of the Kuwaiti liver transplant program poses further challenges, thus sustaining success will be key. Despite being in a state-of-the-art facility, many services that are essential for the program have limited expertise in liver transplantation and continuous exchange with regional or international high-volume programs will therefore be necessary.

With successful outcomes, the number of referrals has increased and the waiting list has grown exponentially. To accommodate these demands, the pool of deceased donors must be expanded. In our region, deceased-donor scarcity is broadly linked to 2 types of concerns: a religious belief, which either rejects donation or limits deceased donation, and a cultural one in which the procurement of organs is considered as an act of body mutilation. To counter these beliefs, public awareness campaigns, especially on social media, have been initiated. While there needs to be an emphasis on deceased donation, establishing a living-donor program will also be necessary. In the interim, we will continue to refer patients with rapid deteriorating liver function requiring an urgent transplant to a regional expert center.

### CONCLUSION

Starting liver transplant programs in low-population countries carries unique challenges that require extraordinary solutions. We started our liver transplant program in Kuwait in collaboration with KCL, in a model that enables the support of the local team without diluting their experience.

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