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ORIGINAL RESEARCH

Transplant Without Borders: Clinical Outcomes and Challenges in Transborder Living Donor Pediatric Liver Transplantation in Jordan

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Purpose: To describe the clinical outcomes, complications, and logistical challenges of pediatric living donor liver transplantation (LT) in Jordanian children referred abroad, in the absence of a national transplant program.

Patients and Methods: This retrospective study reviewed all pediatric cases referred to the Jordanian Center for Organ Transplantation (JCOT) for LT between 2019 and 2023. Data were collected from JCOT records and follow-up interviews with caregivers. Variables included patient demographics, indications for transplantation, donor-recipient relationships, post-operative complications, survival outcomes, and financial aspects.

Results: A total of 31 children were referred for LT, of whom 20 (64.5%) successfully underwent living donor liver transplantation abroad—primarily in Turkey—while 11 (35.5%) remained on the waiting list. Biliary atresia (25%) was the most common indication, followed by Alagille syndrome and progressive familial intrahepatic cholestasis (each 20%). Primary hyperoxaluria, Crigler-Najjar syndrome, and maple syrup urine disease were also observed. Parents were the most frequent donors (70%). The most common complications were bile duct leakage (35%), portal vein thrombosis (20%), and infections (15%). The 5-year post-transplant survival rate was 90%. Among the waiting list group, four children (36.4%) died before receiving a transplant. No children underwent transplantation for pediatric acute liver failure during the study period. The average cost per transplant covered by the Ministry of Health was $61,071, excluding out-of-pocket expenses borne by families.

Conclusion: This study highlights the feasibility and challenges of transborder pediatric liver transplantation in Jordan. While clinical outcomes for transplanted children were favorable, significant barriers remain, including delayed referrals, financial strain, and mortality among waitlisted patients. These findings underscore the urgent need to establish a national pediatric liver transplant program to improve timely access and long-term care for children with end-stage liver disease in Jordan.

Plain Language Summary: In Jordan, children who need liver transplants do not have access to a transplant center within the country. Instead, they must travel abroad—usually to Turkey—for this life-saving surgery. This study looked at how this process works, what challenges families face, and how children do after their transplants.

The researchers reviewed the records of all Jordanian children referred for liver transplantation between 2019 and 2023. They found that 20 children successfully received a transplant abroad, while 11 others were still waiting. The most common reason for needing a liver transplant was a condition called biliary atresia, which blocks bile flow from the liver and can cause liver failure in infants. All transplants were done using living donors, usually a parent.

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Although most children who received a transplant survived and did well, many faced serious complications after surgery, such as bile leakage or infections. Sadly, four children on the waiting list died before they could get a transplant. Families also faced financial and emotional stress due to the travel, paperwork, and long hospital stays.

This study is the first to describe how pediatric liver transplantation works in Jordan under the current system. It shows that while the overseas model can save lives, it also has major challenges. The researchers highlight the urgent need for a national transplant center in Jordan, along with better coordination, earlier referrals, and long-term follow-up care for these children.

Keywords: pediatric hepatology, cross-border healthcare, living donor surgery, organ transplant outcomes, health system barriers, Jordan

Introduction

Liver transplantation (LT) remains the gold standard for treating irreversible liver disease in children.[1] Since the first successful liver transplant in 1967, the field has advanced significantly, leading to a growing number of procedures performed in both adults and pediatric patients worldwide.[2–4] With improvements in surgical techniques and immunosuppressive therapies, the indications for liver transplantation have expanded considerably.[5]

These indications include acute liver failure, end-stage chronic liver disease, metabolic disorders, and certain liver tumors.[6] Common indications include biliary atresia, autoimmune hepatitis, Wilson's disease, and metabolic disorders such as urea cycle defects and hereditary tyrosinemia.[5] Transplantation is necessary when complications arise, metabolic defects cannot be managed otherwise, or tumors are unresectable.[6] The decision is guided by the Pediatric End-Stage Liver Disease (PELD) score, which assesses disease severity in children under 12 years old based on bilirubin, INR, albumin, growth failure, and age.[5]

Although liver transplantation is a life-saving procedure, it carries certain risks, including graft rejection (acute or chronic), infections, vascular and biliary complications, and graft dysfunction.[7] Long-term complications include post-transplant lymphoproliferative disorder (PTLD), renal dysfunction, growth failure, and recurrence of primary liver disease.[7] Liver transplantation can be performed as either a living donor liver transplantation (LDLT) or a deceased donor liver transplantation (DDLT), also known as cadaveric transplantation.[8] LDLT offers advantages such as shorter waiting times, better graft quality, and improved post-transplant outcomes, but it requires rigorous donor evaluation to minimize risks.[9,10] In contrast, DDLT remains the most common approach worldwide, though it is restricted by organ availability.[11]

Globally, liver transplantation has become the definitive therapy for a wide range of irreversible pediatric liver diseases. Each year, thousands of children undergo transplantation, with biliary atresia consistently reported as the leading indication worldwide, followed by metabolic and genetic liver disorders.[2,5,6] Despite advances in surgical techniques and immunosuppression, mortality on the pediatric liver transplant waiting list remains substantial, particularly in low- and middle-income countries where timely access to transplantation is limited.[6,11]

LDLT has emerged as a critical solution to the shortage of deceased donor organs. Compared with deceased donor transplantation, LDLT is associated with shorter waiting times, improved graft quality, and favorable long-term survival outcomes.[8,9] These advantages are especially relevant in countries such as Jordan, where no cadaveric donor program currently exists.[12]

The rationale for the present study lies in the absence of a national pediatric liver transplantation program in Jordan and the lack of published data describing outcomes under the Ministry of Health's transborder referral system. While studies from countries with established programs have described outcomes in their own populations,[2,5,6] such findings cannot adequately reflect the logistical, financial, and clinical challenges unique to the Jordanian context. Our work therefore provides the first national evidence on pediatric liver transplantation in Jordan, highlighting the implications of a cross-border model of care and underscoring the need for establishing a local transplant program.

Pediatric liver transplantation in Jordan remains an underexplored field, with no established national program for the procedure. Consequently, children requiring LT are typically referred abroad for treatment under the Ministry of Health (MOH) insurance coverage, a practice previously used in other countries.[12] This practice started in Jordan in 2019, however, no prior study has examined the outcomes of this referral model in Jordan.

The primary aim of this study was to investigate the indications for and complications after LT in children referred for the procedure outside Jordan. The secondary aim was to assess these children survival rates and the associated treatment costs.

Materials and Methods

This retrospective study reviewed all pediatric cases referred to the Jordanian Center for Organ Transplantation (JCOT) at the Ministry of Health for liver transplantation between January 2019 and December 2023. Data collection and analysis were performed between March and July 2024. Ethical approval was obtained from the Institutional Review Board (IRB) of the Ministry of Health and the University of Jordan School of Medicine Board. This study was conducted in accordance with the principles of the Declaration of Helsinki. All organs were donated voluntarily, with written informed consent obtained from the donors, and the procedures were conducted in line with the Declaration of Istanbul. For follow-up interviews with caregivers, verbal informed consent was obtained, which was reviewed and approved by the Institutional Review Board of the Ministry of Health and the University of Jordan.

The study included all children under the age of 18 who were referred to JCOT for pediatric LT. Cases involving children referred for LT in combination with other organ transplants, such as kidney transplants, were also included. However, children who were referred to JCOT for organ transplantation but remained on the waiting list were excluded from the analysis.

In Jordan, children who require LT are referred to JCOT for evaluation and coordination of the procedure. To proceed with the referral, the child's caregiver must provide three supporting letters from pediatric gastroenterologists (peds GI). These letters must confirm that the child has chronic liver disease, requires a liver transplant, and that the procedure cannot be performed at the referring institution. The letters are issued by specialists from the Royal Medical Services, the Ministry of Health, and Jordan University Hospital.

Once the required documents are submitted, a specialized committee at JCOT reviews all referred cases and determines which children are eligible for LT. Since there is no pediatric liver transplant center in Jordan, the committee decides on the most suitable facility abroad where the child can undergo the procedure. The committee then coordinates with the surgical team in that facility to ensure all arrangements are in place.

After the committee finalizes its recommendations, they are sent to the Ministry of Health, where they must be reviewed and approved by a higher-level body known as the Committee for Insured Citizens' Treatment Abroad. This committee is responsible for making the final arrangements to send the child for LT outside Jordan and for covering the financial costs associated with the surgery.

During the study, medical records at JCOT were reviewed, and clinical data were extracted. Any missing information was obtained through a phone interview with one of the child's parents, during which verbal consent was obtained.

The collected data included children's demographics, the name of the center where the initial diagnosis of liver disease was made, and details related to the transplant process. These details encompassed the indication for LT, the child's age at the time of transplantation, the blood groups of both the donor and recipient, and the degree of relatedness between them. Additionally, any post-transplant complications were documented. Post-transplant follow-up was conducted at the transplant centers abroad. Patients were routinely assessed within the first month after discharge, followed by regular visits every 3 months during the first year and every 6–12 months thereafter, with additional visits as clinically indicated. Immunosuppression regimens were standardized according to the protocols of the receiving transplant centers abroad, with tacrolimus as the mainstay calcineurin inhibitor and adjunctive corticosteroids administered in selected cases. The cost of the LT procedure and the location where it was performed were also recorded. Calculation of Pediatric End-Stage Liver Disease (PELD) scores was not possible because some of the required laboratory values were unavailable in the referral records.

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as means ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. As this study included all available national cases during the defined period, no a priori sample size calculation was performed. Given the descriptive and exploratory nature of the study, post hoc power analysis was not conducted. All data were entered into an Excel spreadsheet and securely stored on a password-protected desktop computer.

Results

Since the launch of the transborder pediatric liver transplantation (LT) model in Jordan in 2019, a total of 31 children have been referred to JCOT. Of these, 20 children (64.5%) successfully underwent liver transplantation abroad (in Turkey), while 11 children (35.5%) remained on the waiting list (Tables 1 and 2, Figure 1).

Table 1 Clinical Characteristics of Children Who Underwent Liver Transplantation (N= 20)

	N (%)
Gender	
Boys Girls	10 (50) 10 (50)
Age at diagnosis: months ± 2SD	2.33 ± 7.93
Age at transplant: years 2SD	3.86 ± 3.06
Weight at time of transplant: Kg ± 2SD	13.57 ± 8.93
Pre-Transplant diagnosis:	
Biliary Atresia	5 (25)
Alagille syndrome	4 (20)
Progressive Familial Intrahepatic Cholestasis (PFIC)	4(20)
PFIC Type 1	2
PFIC Type 2	1
PFIC Type 4	1
Primary hyperoxaluria type 1	3 (15)
Crigler-Najjar syndrome	2 (10)
Maple Syrup Urine Disease (MSUD)	1 (5)
Donor Relation to Recipients	
Father	8 (40)
Mother	6 (30)
Paternal Aunt	2 (10)
Brother	1 (5)
Paternal Uncle	1 (5)
Maternal Uncle	1 (5)
Cousins	1 (5)
Age of donor: years ± SD	37.8 ± SD 8.79
Blood group of Recipient	
A+	12 (60)
O+	7 (35)
B+	1 (5)

(*Continued*)

Table 1 (Continued).

	N (%)
Blood group of Donor	
A+	9 (45)
O+	9 (45)
B-	1 (5)
O-	1 (5)
Centre of initial diagnosis	
Royal Medical Services	7 (35)
University Hospitals	6 (30)
Ministry of Health	5 (25)
Private sector	2 (10)
Length of hospital stay after LT average (IQL)	45.89(25–50)
Post LT visits to transplant center average ± SD	3.3 ± 1.70

Table 2 Clinical Characteristics of Children in the Waiting List for Liver Transplant (N=11)

	N (%)
Gender	
Boys Girls	7(63.6) 4 (36.4)
Pre-Transplant diagnosis:	
Biliary Atresia	5 (45.4)
Autoimmune hepatitis with cirrhosis	2(18.2)
Progressive Familial Intrahepatic Cholestasis type 2 (PFIC2)	1(9.1)
Primary hyperoxaluria type 1	1 (9.1)
Crigler-Najjar syndrome	1 (9.1)
Congenital hepatic fibrosis with ARPCKD*	1 (9.1)
Centre of initial diagnosis	
Royal Medical Services	4(36.4)
University Hospitals	3 (27.2)
Ministry of Health	2 (18.2)
Private sector	2 (18.2)

Abbreviation: *ARPCKD, Autosomal Recessive Polycystic Kidney Disease.

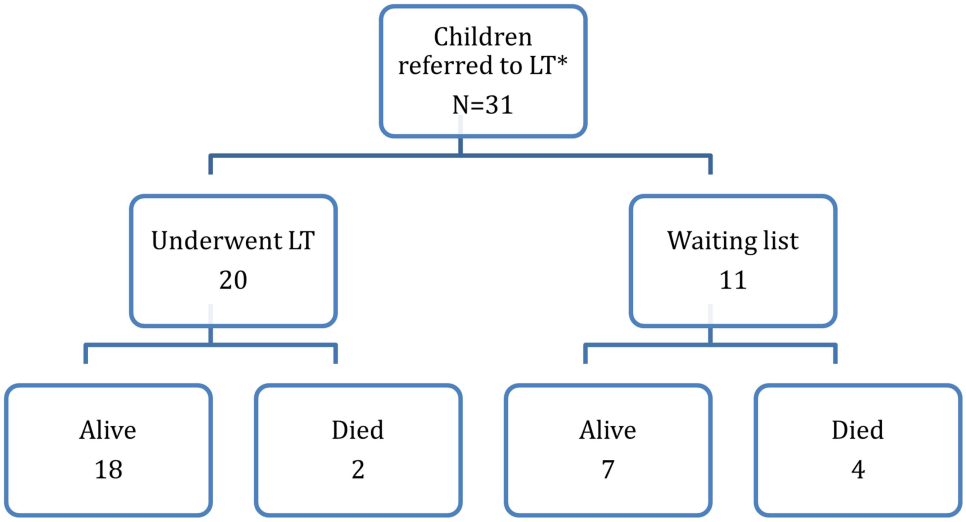

Figure 1 Flow chart of study cohort. *LT: Liver transplant.

Among the 20 transplanted children, the gender distribution was equal with 10 boys and 10 girls. The average age at diagnosis of liver disease was 2.3 months (±7.9 months), and the mean age at LT was 3.86 years (±3.06 years). At the time of transplant, children weighed an average of 13.57 kg (±8.93 kg).

The most common pre-transplant diagnosis was biliary atresia (25%), followed by Alagille syndrome (20%) and progressive familial intrahepatic cholestasis (PFIC, 20%). Of the PFIC cases, type 1 was the most frequent (2 patients), while types 2 and 4 were seen in one child each. Other indications included primary hyperoxaluria type 1 (15%), Crigler-Najjar syndrome (10%), and Maple Syrup Urine Disease (5%).

All patients with biliary atresia had undergone Kasai portoenterostomy in Jordan prior to undergoing LT, with a mean age of 2.4 ± 0.42 months at the time of surgery. At the time of transplantation, the youngest patient was 9 months old, while the oldest was 5 years.

Living donors were used in all cases, with parents serving as donors in 70% of the cases (40% fathers, 30% mothers). Other donors included siblings, uncles, aunts, and cousins. The mean donor age was 37.8 years (±8.79). ABO compatibility was maintained, with A+ and O+ blood groups being the most common among both recipients and donors.

The post-operative complication rate was notable, with bile duct leakage being the most frequent (35%), followed by portal vein thrombosis (20%), bowel perforation (15%), infection (peritonitis/cholangitis, 15%), and ascites (15%) (Table 3). Less common complications included abdominal bleeding, esophageal varices, diaphragmatic hernia, and organ rejection, each affecting one child (5%). Two children developed multiple complications. Sadly, two children (10%) died following transplantation — one due to peritonitis/cholangitis (diagnosed with biliary atresia), and another with hyperoxaluria who died at age of 8 years, four years post-transplant. No complications occurred to the donors post LDLT.

Children required an average of 3.3 follow-up visits (±1.7) at the transplant center abroad, with two patients requiring 12 visits due to complex postoperative courses. The average length of hospital stay after LT was 45.89 days (IQR 25–50).

Analysis of the waiting list group (n=11) revealed a higher proportion of boys (63.6%), with biliary atresia (45.4%) again being the most common indication. Other diagnoses included autoimmune hepatitis with cirrhosis (18.2%), PFIC2, primary hyperoxaluria type 1, Crigler-Najjar syndrome, and congenital hepatic fibrosis with autosomal recessive polycystic kidney disease (each 9.1%). Notably, four children (36.4%) from this group died while waiting for a transplant, including three with biliary atresia and one with PFIC2.

From 2019 to 2023, the number of transplants varied annually, with the highest number (7 cases) performed in 2022 (Table 4). The overall 5-year survival rate was 90%, based on 2 deaths among 20 transplanted children (Figure 2).

Table 3 Complications After Liver Transplantation (N= 20)

Complication	N (%)
Bile Duct Leakage	7 (35)
Portal vein thrombosis	4(20)
Bowel perforation	3 (15)
Infection – peritonitis / cholangitis	3 (15)
Ascites	3 (15)
Abdominal bleeding	2 (10)
Esophageal varices	1 (5)
Diaphragmatic hernia	1 (5)
Umbilical Hernia	1 (5)
Organ rejection – acute	1 (5)

Table 4 Number of Transplant Cases per Year

Year	Number of Transplantation Cases
2019	3
2020	3
2021	3
2022	7
2023	4

The average cost of transplantation, covered by the Ministry of Health, was $61,071 (±$9,440). However, families also incurred additional out-of-pocket expenses, particularly for travel, accommodations, and follow-up care.

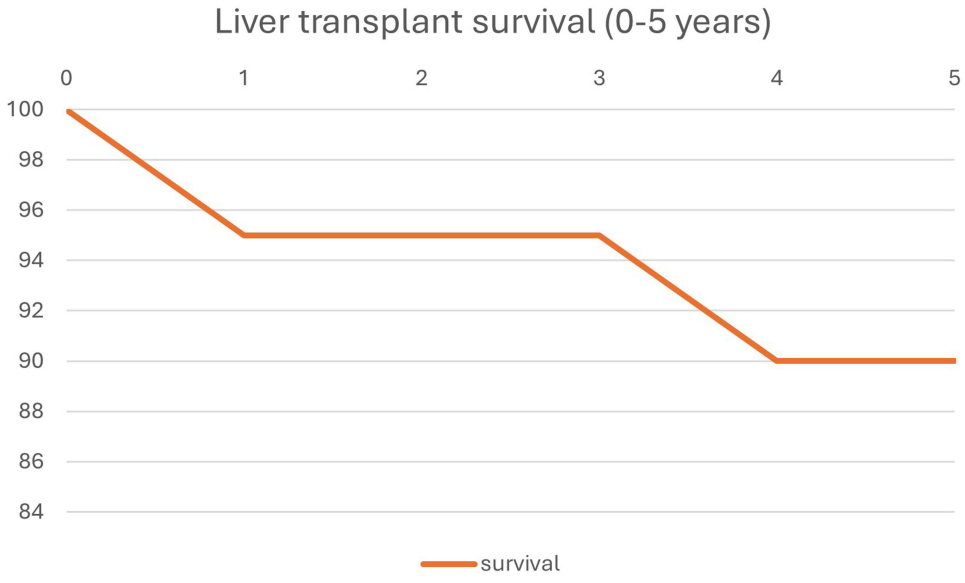

Figure 2 Five-year survival rate post liver transplant.

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Discussion

This study represents the first national report of pediatric LT outcomes in Jordan. It provides novel insights into disease etiology, transplant indications, surgical complications, and survival in a previously undocumented patient population. Prior to this work, there were no published data on pediatric LT in Jordan, and this study thus lays the foundation for future research and national policy development.

The most common indication for transplantation in our cohort was biliary atresia (25%), which aligns with global trends identifying it as the leading cause of pediatric liver transplantation, particularly among infants diagnosed early in life.[2,5] All children with this diagnosis had previously undergone Kasai portoenterostomy in Jordan, suggesting that early surgical management is practiced but often insufficient to prevent disease progression. Progressive familial intrahepatic cholestasis (PFIC) and Alagille syndrome were also prominent, reflecting underlying genetic and syndromic conditions that are known to require transplantation when medical management fails.

All transplants in this cohort were performed using living related donors, with one of the parents acting as the donor in 70% of cases. This mirrors regional reliance on LDLT, especially in countries lacking robust deceased donor programs.[8,9] While LDLT offers benefits such as shorter waiting times and better graft quality, it requires careful donor evaluation and exposes healthy individuals to surgical risk, highlighting the ethical and logistical complexities of relying solely on this modality.[10,11]

The absence of a national pediatric liver transplant center in Jordan means that all procedures are carried out abroad, primarily in Turkey, under a transborder model coordinated by the Ministry of Health. Although effective in providing life-saving treatment, this model presents substantial barriers, including delays in referral, limited follow-up continuity, and financial burdens. Our findings support the urgent need for establishing a national LT center to improve access, continuity of care, and long-term outcomes.[12]

Alarmingly, four children (36.4%) on the waiting list died before undergoing transplantation. This underscores the importance of early identification, faster referral processing, and expanding donor availability. Similar mortality rates among waitlisted children have been reported globally, particularly in settings where access to transplantation is delayed or constrained.[6]

Postoperative complications were frequent and clinically significant, with bile duct leakage (35%), portal vein thrombosis (20%), and bowel perforation (15%) being the most common. These complications mirror those reported in international literature and reflect known risks associated with pediatric LT.[1,7] Two children who developed peritonitis and cholangitis eventually died, highlighting the potentially fatal nature of postoperative infections and the importance of structured post-transplant surveillance. Managing these complications across borders adds another layer of complexity and places further strain on already overstretched healthcare resources, particularly in settings with limited transplant infrastructure.

Despite these complications, the five-year survival rate was 90%, which is comparable to outcomes in developed countries with well-established transplant centers.[5,6] This demonstrates that when transplants are performed in high-volume international centers, outcomes for Jordanian children can match international benchmarks. However, follow-up remains inconsistent. The average number of post-LT visits was 3.3 per patient, with some children requiring more extensive follow-up. Given the need for ongoing immunosuppression, nutritional support, and complication monitoring, structured long-term follow-up remains a critical unmet need.[7]

The economic implications of this care model are also considerable. While the Ministry of Health covered the cost of surgery abroad (Mean $61,071 ± $9440 per child), families were responsible for out-of-pocket expenses related to travel, accommodation, and additional follow-up visits. For many families, this financial burden is substantial and may limit their ability to maintain essential postoperative care. In addition to the economic strain, families must also navigate the bureaucratic burden of obtaining multiple official approvals and paperwork from various institutions, a process that can be time-consuming and emotionally exhausting. These findings align with international experiences where partial state coverage is supplemented by family contributions, creating inequities in access.[11]

The disease etiology in our cohort reflects patterns seen both globally and regionally. In addition to biliary atresia, the relatively high prevalence of PFIC may be attributable to consanguineous marriages, which are common in Jordan and

increase the risk of autosomal recessive liver disorders. This observation supports the need for improved genetic screening, counseling, and early diagnosis.

Interestingly, none of the children in our cohort underwent liver transplantation due to Pediatric Acute Liver Failure (PALF), even though PALF is a well-known and urgent reason for liver transplantation in children.[5,6] This might be due to several reasons. One possibility, although less likely, is that no children with PALF needed LT during the study period. A more likely explanation is that the fast and severe course of PALF did not allow enough time to complete the paperwork and approvals needed to arrange liver transplantation abroad. It is also possible that the medical team did not consider liver transplantation abroad as an option in such emergency cases. Since PALF can worsen very quickly, any delay in referral may lead to missing the chance for a life-saving transplant. This highlights the need to simplify the referral process and raise awareness among healthcare providers about the importance of early recognition and fast action in PALF, especially in countries without local transplant centers.

It is important to note that this study does not capture all children from Jordan who underwent liver transplantation. Some families independently arranged surgeries abroad, especially in Turkey and the United States, through private payment, crowdfunding campaigns, or charitable support. These cases were not documented through the Ministry of Health and were therefore not included in our cohort, suggesting that the true volume and scope of pediatric liver transplantation in Jordan may be underestimated.

Moreover, the fragmented nature of healthcare delivery in Jordan—with diagnoses made across four distinct healthcare sectors—may contribute to variability in referral practices and timing. Centralizing referrals and establishing a national liver transplant registry would help ensure equitable access and standardized evaluation criteria.

In line with our findings, international literature has emphasized the broader implications of cross-border transplantation. Braun et al reported that international travel for liver transplantation introduces complex logistical and ethical challenges, including delays in care, inequities in access, and strain on both sending and receiving healthcare systems.[13] Similarly, Braun and Ascher reviewed domestic and international travel for liver transplantation in the United States, highlighting the impact of transborder care models on patient outcomes and health system resources.[14] These studies reinforce the notion that while cross-border transplantation can be life-saving, it also poses unique risks and underscores the importance of establishing sustainable local transplant programs. Our results echo these observations, as the Jordanian experience demonstrates both the feasibility of transborder referral and the urgent need to build national capacity for pediatric liver transplantation.

This study has several limitations. First, although the data collection period was between March and July 2024, the study cohort actually included all pediatric referrals between 2019 and 2023; nevertheless, the retrospective nature of the study may have introduced reporting bias. Second, the relatively small sample size reflects the national cohort during the study period. While no a priori sample size calculation or post hoc power analysis was performed, the study included all available national cases, which limits the generalizability of findings but ensures representativeness within Jordan. A notable limitation of this study was the unavailability of complete laboratory data, which precluded the calculation of Pediatric End-Stage Liver Disease (PELD) scores. PELD is a validated metric used to assess disease severity and prioritize children for transplantation.[5] The absence of these scores limited our ability to stratify patients by severity or evaluate transplant urgency, which are important considerations in interpreting outcomes. Future studies incorporating routine PELD documentation will provide a more accurate assessment of disease burden and help refine referral practices in Jordan. In addition, there is potential for selection bias, as some families may have independently arranged transplantation abroad outside of the Ministry of Health referral system, and such cases were not captured in our dataset. Finally, while the study provides nationally representative data for Jordan, the findings may not be directly generalizable to other countries with different healthcare systems, transplant infrastructures, or genetic backgrounds. Future studies incorporating routine PELD documentation, larger multi-center cohorts, and national registry data will provide a more accurate assessment of disease burden and help refine referral practices in Jordan.

Given the observed mortality on the waiting list, high complication rates, and reliance on external healthcare systems, there is a clear and pressing need to establish a national pediatric liver transplant center in Jordan. This center should integrate multidisciplinary expertise in pediatric hepatology, surgery, intensive care, nutrition, and infectious diseases. In

the interim, Jordan may benefit from regional partnerships with neighboring countries that have well-developed transplant programs, such as Saudi Arabia or Egypt.[12]

Conclusion

In conclusion, this study provides the first national overview of pediatric liver transplantation in Jordan, offering valuable insights into indications, outcomes, and the limitations of a transborder care model. The findings underscore the urgent need to establish a national pediatric liver transplant center that integrates multidisciplinary expertise and enables timely, equitable care. In the short term, regional collaborations with neighboring countries may offer a feasible bridge. Moving forward, Jordan has the potential to lead in regional transplantation efforts through the development of a national registry, promotion of cadaveric organ donation, and investment in local capacity-building. These steps are essential for improving access, reducing mortality, and ensuring long-term sustainability in pediatric liver transplantation. Future studies should aim to incorporate larger multicenter cohorts, prospective designs, and systematic PELD score documentation to more accurately define disease burden, improve risk stratification, and refine referral practices in Jordan and the wider region.

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Disclosure

The authors report no conflicts of interest, and no financial disclosures related to this work.

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