Original Article

Characteristics and Outcome of Partial Liver Transplant among Pediatrics in a Referral Transplant Center in Iran from 2010 to 2020

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What's Known

- Perioperative characteristics have been identified as significant predictors of outcomes in partial liver transplantation (LT) among pediatric patients.
- Living donor LT has been associated with improved patient survival compared to deceased donor transplantation, highlighting the critical role of donor-recipient matching.

What's New

- This study provided novel insights into the impact of preoperative, intraoperative, and postoperative mortality factors on liver transplantation (LT) outcomes in pediatric patients in Iran. Preoperative factors included age, alanine aminotransferase, and hemoglobin levels. Intraoperative factors were cold ischemia, anhepatic blood loss, and postoperative mortality factors were fresh frozen plasma transfusion, bleeding, bowel perforation, and primary non-function.

Abstract

Background: Liver transplantation (LT) is a critical intervention for pediatric patients with advanced liver failure. This study aimed to assess the impact of perioperative factors on LT outcomes in pediatric patients.

Methods: This retrospective cohort study, conducted from 2010-2020, included 563 pediatric patients who underwent LT in Shiraz, Iran. Most patients received liver grafts from living donors due to cholestatic and metabolic diseases, and all had complete medical and laboratory records. Data were analyzed using various regression models (Cox, linear, and logistic) in SPSS software (version 22).

Results: Of the 563 patients who underwent LT, 436 received livers from living donors and 127 from deceased donors. The primary diagnoses included cholestatic diseases (44.4%) and metabolic diseases (34.1%). Post-transplant rejection and mortality rates were 21.1% (119 patients) and 36.1% (203 patients), respectively. Preoperative factors associated with rejection included weight (HR=1.01, P=0.01) and albumin (HR=0.69, P=0.03). Postoperative factors influencing rejection included platelet transfusion (HR=2.12, P=0.03), primary non-function (PNF) (HR=4.6, P=0.01), cytomegalovirus (CMV)(HR=1.78, P=0.005), and convulsion (HR=1.93, P=0.007). Preoperative factors that affect mortality were age (HR=0.89, P<0.001), alanine aminotransferase (ALT) (HR=1, P=0.047), and hemoglobin levels (HR=0.91, P=0.03). Intraoperative factors influencing mortality included cold ischemia duration (HR=0.98, P=0.048) and anhepatic blood loss (HR=1.02, P<0.001). Postoperative factors associated with mortality included fresh frozen plasma (FFP) transfusion (HR=1.7, P=0.004), bleeding (HR=2.17, P=0.009), bowel perforation (HR=2.55, P=0.01), and PNF (HR=11.24, P<0.001).

Conclusion: Optimizing perioperative care practices could significantly improve LT outcomes in pediatric patients.

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Keywords ● Pediatrics ● Liver transplantation ● Mortality ● Graft rejection ● Reperfusion

Introduction

Advances in medical sciences have significantly increased the life expectancy of patients suffering from organ failure and end-stage organ disease, including those with liver failure.[1] Liver

transplantation (LT) has emerged as one of the most effective treatment strategies to improve survival rates in patients with advanced liver failure,[2] particularly in pediatrics. Common indications for LT in pediatric patients include cholestatic diseases, metabolic disorders, acute liver failure due to viral infections or drug toxicity, chronic hepatitis, and malignancies.[3]

LT has proven to be a successful treatment for children with end-stage liver disease, offering them the opportunity for a long and healthy life. However, organ scarcity remains a significant limitation to the widespread application of transplantation. This challenge has been partially addressed through innovative surgical techniques, such as split-liver and living-donor transplantation. These advancements have significantly reduced waiting list mortality, particularly for pediatric patients, who historically faced higher mortality rates than adults during the 1980s and 1990s.[4]

In the United States, pediatric LT accounts for about 7% to 8% of all LTs, with around 500 cases performed annually. The majority of these transplants were performed on children under two years of age, with another peak in adolescence.[5]

Despite these advancements, pediatric LT surgeries are associated with various surgical and anesthesiologic complications, necessitating thorough evaluation of potential perioperative risk factors.[6] According to the US Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients, the 1-year survival rate after LT ranged from 83% to 91%, while the 5-year survival rate ranged from 82% to 84%.[7]

Based on the high number of LT cases in Iran, this study aimed to evaluate the effect of perioperative characteristics on the LT outcome, including rejection rates, mortality rates, pediatric intensive care unit (PICU) stay duration, post-operative intubation period, and reperfusion syndrome. The study focused on pediatric patients in Abu-Ali Sina Hospital (Shiraz, Iran), as the largest transplantation single center outside the United States and the main referral center for pediatric LT in Iran.

Patients and Methods

This retrospective cohort study assessed clinical and laboratory records of all pediatric patients under 18 years of age who underwent partial LT (from both cadaveric and living donors) at Abu-Ali Sina Hospital, Shiraz, Iran, from 2010 to 2020. The present study was approved by the Ethics Committee of Shiraz University of Medical Sciences (code: IR.SUMS.MED.REC.1400.300). Due to the retrospective nature of the study, the requirement for informed consent was waived by the Ethics Committee of Shiraz University of Medical Sciences. The patient's information was anonymized before analysis, and the researchers ensured the confidentiality of all data.

All the patients' medical and laboratory records were extracted and reviewed from the hospital's electronic inpatient medical record databases. Demographic data, such as age, sex, weight, body mass index (BMI), etiology of end-stage liver disease, model for end-stage liver disease (MELD) score, and previous admission history, were recorded. The laboratory data and the perioperative features, such as the LT technique, mean operation time, type of transplantation, post-reperfusion syndrome (PRS), length of stay in the pediatric intensive care unit (PICU), hospital stay, readmission rates, rejection or re-transplantation episodes, and clinical outcomes after transplantation, were also evaluated. Mortalities included in-hospital mortalities and those occurring during regular follow-up visits.

Statistical Analysis

Data were analyzed using SPSS software (version 22, SPSS Inc., Chicago, IL). Continuous variables were reported as median (Q_1-Q_3), and categorical variables were summarized using numbers and percentages. Univariate and multiple Cox regression analyses with the backward LR method were used for multivariate survival analysis. Univariate and multiple linear regression analyses were applied to variables with continuous responses, and univariate and multiple logistic regression analyses were used for the binary response. Significant variables from the univariate and full models were included in the multiple logistic model. The significant variables from the final model were then reviewed for clinical relevance by clinical experts and reported as the best logistic model. $P<0.05$ was considered statistically significant.

Results

In this study, 563 patients underwent LT, of whom 436 pediatrics (77.4%) received a liver from a living donor, and 127 (22.6%) received a liver from a deceased donor. The most common diagnoses among the 563 transplant recipients were cholestatic diseases (44.4%) and metabolic liver diseases (34.1%). The majority of patients were under 4 years of age, with a median age at transplantation was 3 years (range=1-7) years. This cohort included 326 (58%) boys and 237 (42%) girls. Post-transplant rejection and

mortality rates were 119 (21.1%) and 203 (36.1%), respectively (table 1). The median follow-up time was 789 (range=129-2369) days.

Univariate and multiple Cox regression were performed to identify significant variables affecting rejection and mortality of patients. As shown in table 2, preoperative factors significantly influencing rejection included patients' weight and serum albumin levels. The hazard of rejection increased by 1% for every Kg weight gain (P=0.012) and decreased by 30% with one g/dL of increased albumin (P=0.033). Preoperative factors affecting mortality rate included age, alanine aminotransferase (ALT), and hemoglobin levels. The mortality hazard decreased by 11% for each additional year of age (P<0.001). For ALT, a 1 U/L increase was associated with a marginal increase in mortality hazard (P=0.047), and a 1 g/dL increase in hemoglobin reduced the hazard by 9% (P=0.03).

Table 1: Patient characteristics

Variables		Total patients n=563
Age		3 (1-7)
Sex	Male	326 (58)
	Female	237 (42)
Weight (Kg)		12 (9-22)
BMI (Kg/ m^2)		16.9 (14.5-20)
MELD score		19 (14-25)
Liver Disease	Cholestasis	250 (44.4)
	Metabolic	192 (34.1)
	Cryptogenic	30 (5.3)
	Autoimmune hepatitis	19 (3.4)
	Neonatal hepatitis	25 (4.4)
	Acute liver failure	10 (1.8)
	Congenital hepatic fibrosis	3 (0.4)
	Tumor	15 (2.7)
	Budd-Chiari	3 (0.5)
	Necrosis	5 (0.9)
	other causes	11 (2)
Donor	Alive	436 (77.4)
	Deceased	127 (22.6)
Mortality	Yes	203 (36.1)
	No	360 (63.9)
Rejection	Yes	119 (21.1)
	No	444 (78.9)

MELD: Model for end-stage liver disease; The values indicate frequency (percentage) or median (Q_1-Q_3).

Table 2: Summary of significant clinical features of liver transplant in multivariate survival analysis

Time	Event	Significant variable	HR	95% CI	P value
Pre-operative	Rejection	Weight (Kg)	1.01	(1.00-1.03)	0.012*
		Albumin (g/dL)	0.69	(0.49-0.97)	0.033*
	Mortality	Age (year)	0.89	(0.85-0.94)	≤0.001*
		ALT (U/L)	1	(1-1)	0.047*
		Hemoglobin (g/dL)	0.91	(0.85-0.99)	0.03*
Intra-operative	Rejection	-	-	-	-
	Mortality	Cold ischemia duration(hour)	0.98	(0.97-1)	0.048*
		Anhepatic blood loss(mL/Kg)	1.02	(1.01-1.04)	≤0.001*
Post-operative	Rejection	Platelet Transfusion (unit)	2.12	(1.30-3.47)	0.03*
		Primary non-function	4.6	(1.38-15.43)	0.01*
		CMV (IU/mL)	1.78	(1.19-2.67)	0.005*
		Convulsion	1.93	(1.19-3.12)	0.007*
	Mortality	FFP Transfusion (mL)	1.70	(1.18-2.46)	0.004*
		Bleeding (mL)	2.17	(1.20-3.71)	0.009*
		Bowel perforation	2.55	(1.17-5.53)	0.01*
		PNF	11.24	(6.67-18.93)	≤0.001*

HR: Hazard ratio; CI: Confidence interval; ALT: Alanine aminotransferase; CMV: Cytomegalovirus; PNF: Primary non-function
*Indicates significant P values; Multiple Cox regression was used; P<0.05 was significant.

Among intraoperative factors, cold ischemia duration and anhepatic phase blood loss (mL/Kg) significantly affected mortality. Each additional minute of cold ischemia duration reduced the mortality hazard by 2% (P=0.048), while each mL/Kg increase in anhepatic blood loss increased the hazard by 2% (P<0.001). Postoperative factors significantly associated with rejection included platelet transfusion, primary non-function (PNF) of the liver, cytomegalovirus (CMV) infection, and convulsion. The rejection hazard increased more than twice with platelet transfusion (P=0.03). The existence of PNF increased the rejection hazard by 4.6 times (P=0.01). CMV infection increased the hazard by 78% (P=0.005), and each convulsion increased it by 93% (P=0.007). Postoperative factors influencing mortality included fresh frozen plasma (FFP) transfusion, bleeding, bowel perforation, and PNF. FFP transfusion increased the mortality hazard by 70% (P=0.004), while post-operative bleeding doubled the hazard (P=0.009). Bowel perforation increased the hazard by 2.5 times (P=0.01), and PNF increased it by more than 11 times (P<0.001).

Significant clinical features associated with the duration of PICU admission and post-operative intubation were identified using multiple linear regression (Table 3). The MELD score, necrotic liver disease, blood sugar level, the grafted liver weight of patients in preoperative features, duration of operation, cold and warm ischemia duration, and hepatectomy phase blood loss (mL/Kg) among intraoperative features were associated with the period of PICU admission. Necrotic liver disease (β=0.24) in preoperative and hepatectomy blood loss (mL/Kg) (β=0.16) in intraoperative had the highest impact on the PICU admission period. Among postoperative features, infection (β=0.28), pneumonia (β=0.22), and intubation period (β=0.21) had the highest effect on the PICU admission period, respectively. However, PNF (β=-0.15) reduced the length of stay in the PICU. Preoperative factors associated with post-operative intubation duration included cryptogenic liver disease, tumors, and elevated direct bilirubin levels. Among intraoperative features, anhepatic time and short duration of warm ischemia were related to the postoperative intubation period. The PICU stay duration, platelet transfusion, convulsion, and pneumonia were associated with the intubation period after LT surgery. The existence of tumor (β=0.59),

Table 3: Summary of significant clinical features of liver transplant in multiple linear regression for the best model of PICU admission period and intubation period

Time	Response variable	Significant variables	β^{US}	$S.E^{US}$	β^{S}	P value
Pre-operative	PICU admission period	MELD score	0.25	0.09	0.14	0.04*
		Necrosis	24.97	7.18	0.24	≤0.001*
		Blood sugar	0.05	0.02	0.16	0.02*
		Grafted Liver weight(g)	-0.09	0.005	-0.02	0.003*
	Intubation period	Cryptogenic	14.78	5.17	0.15	0.04*
		Tumor	616.83	70.36	0.59	≤0.001*
		Direct Bilirubin	3.99	1.31	0.23	0.002*
Intra-operative	PICU admission period	Duration of operation	-0.03	0.01	-0.15	≤0.001*
		Cold ischemia duration	0.04	0.01	0.14	0.001*
		Warm ischemia duration	-0.14	0.07	-0.09	0.049*
		Hepatectomy blood loss (mL/Kg)	0.19	0.05	0.16	≤0.001*
	Intubation period	Warm ischemia duration	-4.41	1.29	-0.27	0.003*
		Anhepatic time	5.34	0.52	0.85	≤0.001*
Post-operative	PICU admission period	Intubation period	0.02	0.006	0.21	≤0.001*
		Fluid Therapy in day 7 after OP ([mL/Kg]/24 h)	0.44	0.08	0.13	0.02*
		Infection	9.94	1.85	0.28	≤0.001*
		Biliary Leak	21.78	6.90	0.18	0.001*
		Pneumonia	12.91	3.29	0.22	≤0.001*
		PNF	-20.14	8.12	-0.15	0.02*
		Rejection	5.18	2.19	0.13	0.02*
	Intubation period	Admission duration PICU	1.58	0.46	0.20	≤0.001*
		Platelet Transfusion	79.84	17.66	0.25	≤0.001*
		Convulsion	57.54	20.25	0.15	0.005*
		Pneumonia	56.12	28.48	0.11	0.05*

MELD: Model for end-stage liver disease; PICU: Pediatric intensive care unit; PNF: Primary non-function; The value of β^{S} is standardized, and the value of β^{US} and $S.E^{US}$ are unstandardized. The stepwise multiple regression method was used. *Indicates significant P values. P<0.05 was significant.

Table 4: Summary of significant clinical features of liver transplant in multiple logistic regression for the best model of reperfusion syndrome

Time	Response variable	Significant variables	RR	95% CI	P value
Pre-operation	Reperfusion syndrome	Direct Bilirubin (mg/dL)	0.95	(0.91-0.99)	0.01*
		Hemoglobin (g/dL)	1.17	(1.03-1.35)	0.01*
Intra-operative	Reperfusion syndrome	Hepatectomy blood loss (mL/Kg)	0.84	(0.74-0.95)	0.007*

RR: Relative risk; Multiple logistic regression was used; *Indicates significant P values; P<0.05 was significant.

anhepatic time (β=0.85), and platelet transfusion (β=0.25) had the highest impact on the postoperative intubation period. In contrast, warm ischemia duration (β=-0.27) was associated with a reduction in the intubation period.

Table 4 summarizes significant clinical features associated with reperfusion syndrome. Elevated direct bilirubin levels decreased the chance of reperfusion syndrome by 5%, and low hemoglobin levels increased it by 17%. Hepatectomy blood loss (mL/Kg) during the operation reduced the chance of reperfusion syndrome by 16%. These findings suggested that monitoring direct bilirubin and hemoglobin levels prior to transplantation might help mitigate the risk of reperfusion syndrome.

Discussion

The prognosis and outcome of LT in pediatric patients remain a critical issue. In our 11-year evaluation of partial pediatric LT recipients, a mortality rate of 36.1% and a rejection rate of 21.1% were observed, which aligned with findings from other studies. A nationwide study in Iran by Malek-Hosseini and colleagues reported overall survival rates of 76%, 67%, and 56% at 1, 5, and 10 years, respectively, for pediatric LT recipients.[8] Similarly, Bahador and colleagues reported a mortality rate of 27.5%, with 26.1% occurring as in-hospital mortality among pediatric orthotopic liver transplantation (OLT) cases in Iran from 1999 to 2008.[9] A previous study at our center, encompassing all types of pediatric LT, demonstrated a mortality rate of 21.1% from 2000 to 2011.[10] In contrast, the society of pediatric liver transplantation (SPLIT) registry reported a higher rejection rate of 46% while a mortality rate of 12% among pediatric LT.[11] Merion and colleagues reported that split LT resulted in 3.7 months of extra life for the pediatric recipient, with a re-transplant rate twice as high as that for whole organ recipients.[12] Long-term survival data from other transplant centers indicated increased survival rates over time, attributed to earlier patient referrals, advancements in surgical techniques, enhanced perioperative management, and a better understanding of more potent immunosuppressive agents.[13] Collectively, these studies underscored that pediatric LT is still a procedure associated with relatively high mortality rates. Therefore, the present study aimed to improve the patients' management by identifying factors correlated with outcomes and prognosis through regression model analysis. It was found that preoperative factors such as older age, higher ALT levels, and lower hemoglobin levels were associated with an increased risk of mortality. Specifically, each additional year of age was associated with an 11% reduction in mortality hazard, while each 1 U/L increase in ALT was associated with a marginal increase in mortality hazard. Conversely, each 1 g/dL increase in hemoglobin was associated with a 9% decrease in mortality hazard. Among intraoperative factors, increased cold ischemia duration was associated with a 2% decrease in mortality hazard per additional minute, while each mL/Kg of anhepatic blood loss was associated with a 2% increase in mortality hazard. Postoperative factors significantly associated with increased mortality included FFP transfusion (70% higher mortality hazard), postoperative bleeding (2-fold higher mortality hazard), bowel perforation (2.5-fold higher mortality hazard), and primary non-function (over 11-fold higher mortality hazard).

Over the 11-year study period, 463 patients (77.4%) received a liver from a living donor, and 127 patients (22.6%) received a liver from a deceased donor. The most common diagnoses were cholestatic (44.4%) and metabolic liver diseases (34.1%). Candidates for LTs often present with concurrent medical conditions that may complicate anesthesia and require comprehensive preoperative evaluation. One of the advantages of living donor LT is the opportunity for comprehensive assessment and optimization of the recipient's concurrent conditions shortly before the procedure, given its elective nature. This allows for timely management of medical issues that could otherwise impact outcomes. In contrast, evaluations for deceased donor LT were typically conducted when patients were placed on the waiting list, and these assessments might become outdated by the time a suitable donor becomes available. The urgency of deceased donor LT often precludes the possibility of reassessing or addressing these conditions prior to surgery.[14]

Based on the findings of the present study, preoperative hemoglobin levels were significantly correlated with mortality, with each 1 g/dL increase in hemoglobin associated with a 9% reduction in mortality hazard. Conversely, postoperative FFP transfusion increased the mortality hazard by 70%, and the rejection hazard increased more than twice with postoperative platelet transfuse. The primary goal of blood and fluid replacement therapy is to provide an adequate circulatory function rather than a rigid replacement of genuine blood loss. However, accurately assessing blood loss during LT was challenging, as traditional methods such as measuring surgical suction and weighing sponges might overestimate erythrocyte loss due to excessive transudation into the peritoneal cavity.[15] Blood loss during LTs is highly variable, and severe bleeding is a well-recognized complication. Massive bleeding and transfusion of banked blood can lead to acute hypovolemia, citrate-induced ionized hypocalcemia, hyperosmolality, and hypothermia. Numerous studies established a strong association between massive blood transfusions and increased postoperative morbidity and mortality. In adult LT recipients, transfusions were suggested to be associated with worse outcomes.[16] Nevertheless, predicting intraoperative bleeding during orthotopic LTs remained difficult due to the multitude of uncontrolled variables that might influence blood loss.[17]

The immediate postoperative period following LT, particularly during the patient's stay in the intensive therapy unit (ITU), is associated with the highest morbidity and mortality.[18] Consequently, ITU management, along with refined surgical timing and technique, is expected to play a pivotal role in optimizing outcomes. Gaschow and colleagues reported that the ICU post-operative period accounted for 76.7% of all fatalities,[19] which was consistent with the findings of another previous study.[20] These results underscored the importance of multidisciplinary, high-level intensive care management. It is widely recognized that the recipient's clinical status during LT significantly influences outcomes.[21] Our study identified several factors associated with prolonged ITU admission. Preoperative factors included the MELD score, necrotic liver disease, blood glucose levels, and graft liver weight. Intraoperative factors included operation duration, cold and warm ischemia duration, and hepatectomy blood loss (mL/Kg). Among these, necrotic liver disease (preoperative) and hepatectomy blood loss (intraoperative) had the greatest impact on ITU admission duration. Postoperative factors such as infection, pneumonia, and intubation duration further prolonged ITU stays. Notably, PNF was associated with a reduced ITU length of stay. Aside from the features that are recipients based and could be considered before the operation, intraoperative factors such as operation duration, cold and warm ischemia duration, and hepatectomy blood loss were associated with intraoperative factors with prolonged ITU duration, which could be improved with the enhanced surgical expertise and refined perioperative protocols.

PRS is a life-threatening and relatively common complication of LT. A study by Zhang and colleagues reported a PRS incidence of 34.7% among 75 pediatric patients receiving deceased donors LT from July 2015 to October 2017. In their study, risk factors for PRS included graft-to-recipient weight ratio, donor warm ischemia time, the use of an expanded criteria donor liver graft, and lower hematocrit level before reperfusion.[22] In contrast, Sahmeddini and colleagues observed a 33% PRS incidence in adult LT recipients at our center,[23] with age>60 years, higher MELD score, Child-Pugh scores C, prolonged cold ischemic time, preoperative sodium< 130 mmol/L, and use of the classical surgical technique as predictive factors for reperfusion syndrome. In our study, among the pediatric population, a lower incidence of reperfusion syndrome was associated with higher preoperative direct bilirubin levels, higher hemoglobin levels, and reduced hepatectomy blood loss (mL/kg) during the operation.

Based on the findings of the present study, a high level of direct bilirubin decreased the chance of PRS by 5%, while preoperative hemoglobin levels increased the risk by 17%. Hepatectomy blood loss (mL/Kg) during the operation reduced the chance of PRS by 16%. Current evidence on PRS risk factors is still limited, particularly in pediatric populations, underscoring the need for multicenter studies to validate these findings and elucidate underlying mechanisms.

Another critical factor explored in this study was the duration of the postoperative intubation in pediatric LT patients. Preoperative factors influencing prolonged intubation included cryptogenic liver disease, tumors, and elevated direct bilirubin levels. Intraoperative factors such as prolonged anhepatic time and short duration of warm ischemia were also associated with extended intubation. Postoperatively, prolonged stays in PICU, platelet transfusion, convulsion, and pneumonia further contributed to increased intubation duration. Among these variables, the existence of preoperative tumor, intraoperative anhepatic time, and post-operative platelet

transfusion had the strongest influence on prolonging intubation. Notably, shorter warm ischemia duration was associated with reduced intubation time. Prolonged intubation might increase ventilator-associated morbidity, extend ITU and hospital stays, and elevate healthcare costs. A previous study reported that lower postoperative duration of intubation was associated with lower bacterial infection.[24] Fullington and colleagues demonstrated that immediate extubation after pediatric LT was a safe procedure without compromising patient outcomes.[25] Overall, it is clear that all attempts should be made to minimize intubation duration to improve postoperative prognosis and reduce morbidity.

In this study, postoperative complications were strongly associated with mortality. Postoperative bleeding doubled the mortality hazard, while bowel perforation increased it by 2.5-fold. Finally, the PNF of the graft increased the mortality hazard by more than 11-fold. Complications arising from the technical challenges remain prevalent within the first 6 months following pediatric OLT.[26] Aydogdu and colleagues found that, despite the smaller donor vessels on which to perform anastomosis in the living donor grafts, compared to cadaveric donor grafts, post-transplant technical complications were less common, including hepatic artery thrombosis. This disparity could be explained in part by the development of microvascular techniques.[27] Technical complications such as vascular thrombosis, biliary leaks, and strictures frequently result in bacterial and fungal infections, contributing to a prolonged ITU stay, a risk factor for infection after OLTs.

Postoperative bacterial infections, a leading cause of morbidity and mortality in pediatric LT, were also prevalent and could be life-threatening. The present study demonstrated that infection significantly correlated with prolonged ITU admission duration. Two studies in our center including Pooladfar and others (54.3% bacterial infection rate among 94 LT recipients) and Vazin and colleagues (67.9% incidence in pediatric LT recipients from 2019 to 2020), corroborate these findings.[28, 29] Similarly, the SPLIT database identified infection (28.3%) and cardiopulmonary complications (17%) as the most common causes of death, among 1092 pediatric LT recipients.[30] Besides, postoperative vascular complications (42.9%) and primary graft dysfunction (25.6%) were the leading causes of early graft failure (within 30 days).[30] Infectious complications were well documented as a cause of significant morbidity and mortality following various immunosuppressive conditions, such as OLTs.[31-33]

According to the findings of the present study, PNF was a significant cause of mortality, rejection, and prolonged ITU admission duration. A recent analysis of the European Liver Transplant Registry reported a cumulative PNF incidence of 6% within 90 days post-LT,[34] while a previous study of the same registry (using a 30-day cutoff point) attributed 3% of post-transplant mortality to PNF.[35] Kemmer and colleagues reported that the prevalence of PNF in the United States was comparable to that in Europe.[36] Other investigations found discrepancies in the reported cumulative incidence of PNF.[37-39] This study had several limitations. PNF was initially defined as primary graft failure that necessitated retransplantation or mortality within 30 days of a primary LT. Even though PNF was first observed more than two decades ago, there is still no consensus on how to define it. As a result, the prevalence of PNF varies with the term utilized. Furthermore, the data for this study were collected prior to the Coronavirus pandemic, which resulted in major changes in patient selection and the waiting list. At the same time, the management of transplant patients was implemented.[40, 41] Overall, the pediatric population is one of the most vulnerable groups, and their quality of life can easily be altered based on therapeutic and surgical interventions, environmental factors, and acquired diseases. Therefore, proper risk evaluation of causative and effective factors in these populations is critical to avoid long-term consequences.

Conclusion

Despite advancements in surgical and medical care, several variables remained an important cause of mortality in these patients. A decrease in PICU stay duration and postoperative intubation period could also decrease the medical burden on the patient and healthcare system. Overall, these findings of pediatric LT contributes to the body of knowledge and highlights the need for more prospective studies.

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Authors' Contribution

P.V, M.B.Kh, M.H.E, N.A, M.A.S, F.Kh, S.Gh.T, H.N, A.Sh, K.K, S.S.N, S.N and S.A.M: conception and design; acquisition, analysis, or

interpretation of data for the work, drafting and revising. All authors have read and approved the final manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Naeimehossadat Asmarian and Mohammad Ali Sahmeddini, as the Editorial Board Members, were not involved in any stage of handling this manuscript. A team of independent experts was formed by the Editorial Board to review the article without their knowledge.

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