

Received: 2020.02.24

Accepted: 2021.05.17

Available online: 2021.06.18

Published: 2021.07.06

# Liver Transplantation: A 10-Year Low-Volume Transplant Center Experience in Kazakhstan

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**Background:** Liver transplantation is considered to be the best available treatment option for patients with liver failure. In Kazakhstan, the liver transplantation program was established a decade ago. In this study, we analyzed a low-volume transplant center experience of liver transplantation in Kazakhstan.

**Material/Methods:** Clinical data of the 64 consecutive liver transplantations from deceased and living donors between 2010 and 2020 were retrieved from electronic records. All data were retrospectively analyzed.

**Results:** A total of 64 liver transplantations, 11 from deceased donors and 53 from living donors, were carried out in our center between 2010 and 2020. The mean age of the recipient was 44 years, 53% were female, and 47% were male. Hepatitis B+hepatitis D infection was the most common cause of end-stage liver disease (21 cases; 32.8%). The overall patient survival rates for 1, 3, and 5 years were 75%, 69.5%, and 59.6%, respectively, for recipients of a liver transplant from a living donor and 54.5%, 45.5%, and 39% for recipients of a liver transplant from a deceased donor.

**Conclusions:** Our clinical outcomes had a high rate of biliary and vascular complications that led to a low survival rate of the recipients. Starting the transplant program in Kazakhstan faced various challenges. In the early period, most transplantations were performed in collaboration with or under the guidance of transplant teams from Russia, Turkey, and South Korea. Improving surgical techniques and protocols of pre- and posttransplantation management could reduce the complications after transplantation.

**Keywords:** End Stage Liver Disease • Liver Transplantation • Living Donors

**Full-text PDF:** <https://www.annalsoftransplantation.com/abstract/index/idArt/931786>



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## Background

Liver transplantation is the only treatment option for patients with end-stage liver disease (ESLD) [1]. According to the Republican Center for the Coordination of Transplantation of the Ministry of Health of the Republic of Kazakhstan, 127 adults and 8 children are currently registered on the waiting list for liver transplantation [2]. The first successful deceased donor liver transplantation (DDLT) in Kazakhstan was performed in 1996. However, due to the lack of trained transplant surgeons and immunologists, and especially the absence of deceased donor organs, the first case was the only case for almost 10 years. Asian countries have the lowest rate of liver transplantation from deceased donors. By 2010, the rate of deceased organ donation was 0.05-6.0 per million on a population basis, while in the United States it was 33.9 per million [3]. Currently, the organ transplantation program in Kazakhstan is in its early stages. Similar to other Eastern countries, developing transplant services has met a variety of obstacles. An absence of education regarding the importance of organ donation and transplantation is common, alongside a lack of governmental support and poorly developed health care system, and these factors create a barrier for deceased organ donation development [4-6]. Thus, a notable discrepancy exists between the availability of organs and the patients awaiting liver transplantation in Kazakhstan. Living donation is the most attractive option in solving the organ shortage problem [7]. In Kazakhstan, the first successful liver transplantation from a living donor was performed in 2011 in collaboration with a transplant team from Belarus [8]. Since 2013, liver transplantation numbers have been steadily increasing in transplant

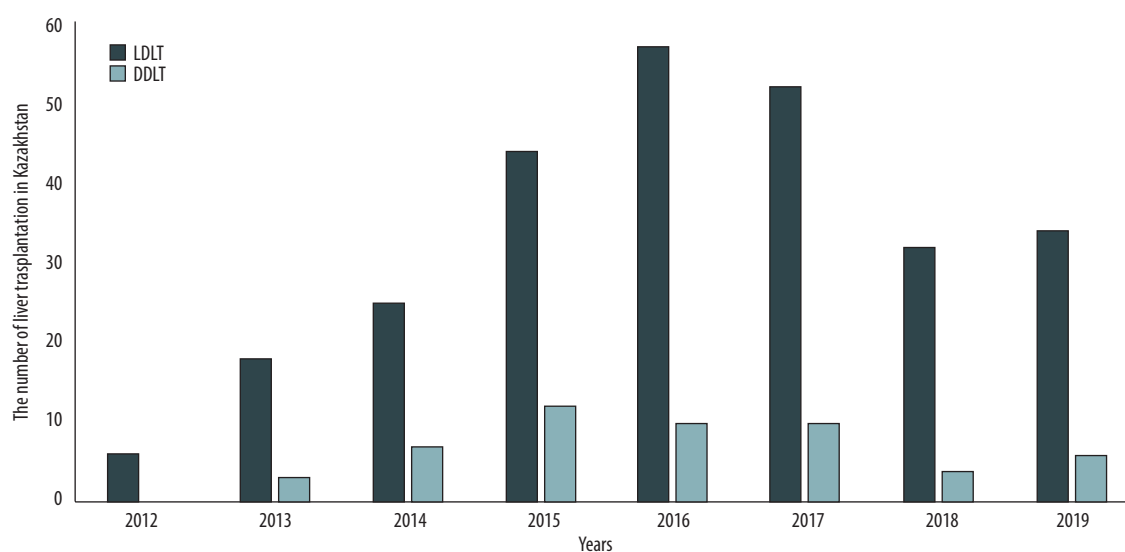
centers of Kazakhstan (Figure 1). In Kazakhstan, live donor liver transplantation (LDLT) accounted for 80% of the total liver transplantation cases in 2019. Here, we present a 10-year single-center experience of liver transplantation in a low-volume transplant center in Kazakhstan.

## Material and Methods

This retrospective study was conducted in compliance with the principles of the Declaration of Helsinki. The Local Ethics Committee of National Research (permit number #7) approved this study.

A total of 64 liver transplantations were performed in our center between January 2011, when the transplant program started in Kazakhstan, and October 2020. Of these transplantations, 11 were from deceased donors and 53 were from living donors. All data concerning recipients and donors were retrieved from electronic data, and we reviewed the course of the recipients. The follow-up period was more than 1 year in all cases. All recipients who received liver transplantation from a deceased or living donor were listed in the National Waiting List of the Republic of Kazakhstan.

Almost all grafts from living donors were right lobe hepatectomy, except 1 left hepatectomy. In all right hepatectomy cases, the middle hepatic vein was left in the donor remnant liver. Remnant liver volume, evaluated by computed tomography, was more than 35%, and graft-to-recipient body weight ratio >0.8 was acceptable in our center. An interposition synthetic



**Figure 1.** Total transplantation cases and proportion of living/deceased donor liver transplantation (LDLT/DDLT) in all transplant centers of Kazakhstan from 2012 to 2019.

**Table 1.** Demographics and clinical characteristics of liver recipients.

Variable	Mean (SD)	Median (range)	N (%)
Age	44 (11)	46.5 (15-63)	64
Gender (Male/Female)			30 (47)-34 (53)
Cause of ESLD			
PBC			9 (14)
HCV			4 (6.35)
HBV			9 (14)
AIH			7 (10.9)
HCC			2 (3.17)
HBV+HDV			21 (32.8)
HBV+HDV+HCV			1 (1.6)
Cryptogenic cirrhosis			4 (6.3)
NASH			3 (4.7)
Others			4 (6.3)
MELD (points)	16 (6)	15 (6-34)	64
Child-Pugh classification			
A			5
B			31
C			28
Bilirubin (µmol/l)	135.01 (141.6)	136.8 (14.4-434)	64
Creatinine (µmol/l)	62.69 (22.8)	63.4 (30-143.75)	64

BMI – body mass index; ESLD – end-stage liver disease; PBC – primary biliary cirrhosis; HCV – hepatitis C virus; HBV – hepatitis B virus; AIH – autoimmune hepatitis; HCC – hepatocellular carcinoma; NASH – non-alcoholic steatohepatitis; MELD – model of end-stage liver disease.

graft was used for venous drainage of segments 5 and 8. Biliary reconstruction was completed either with duct-to-duct anastomoses or with hepaticojejunostomy.

Basiliximab (anti-interleukin-2 receptor antagonist) was used for induction therapy. For mainstay therapy, a calcineurin inhibitor-based immunosuppressive regimen was used in our center. Three-component therapy involved tacrolimus, steroid, and mycophenolate mofetil.

Oral nucleoside analogs were used in recipients with hepatitis B virus (HBV)-associated ESLD prior to liver transplantation and continued after liver transplantation as prophylaxis against recurrence.

The demographic and medical data of participants were analyzed retrospectively. Information on the age of recipients and donors, sex of recipients and donors, donor type, the causes of liver cirrhosis, hospital stay length, postsurgical complications, cold ischemic time, operation time, and bleeding volume is presented in **Tables 1-3**. The overall survival was defined as

the time between the diagnosis date and death or the last follow-up visit. The difference between groups was considered significant if the *P*-value was <0.05. STATA 14.0 software was used to perform the statistical analyses.

## Results

Among 64 liver transplantations, 11 liver grafts were from deceased donors and 53 were from living donors (50 donors were relatives of the recipient, 3 were unrelated donors). There was 1 LDLT from an ABO-incompatible donor. The major causes of liver cirrhosis were hepatitis B and D in 21 cases (32.8%), hepatitis B in 9 (14%), primary biliary cirrhosis in 9 (14%), autoimmune hepatitis in 7 (10.9%), hepatitis C in 4 cases (6.3%), nonalcoholic steatohepatitis in 3 cases (4.7%), and hepatitis B, C, and D in 1 case (1.5%). In 2 cases, hepatocellular carcinoma was an indication for liver transplantation. Cryptogenic cirrhosis (6.3%) and Chananin-Dorfman syndrome (1.6%) were rare indications for liver transplantation.

**Table 2.** Demographics and clinical characteristics of liver donors.

Variable	Mean (SD)	Median (range)	N (%)
Age	32.5 (9.26)	36.5 (22-54)	64
Gender (Male/Female)			45 (70.35)/19 (29.7)
Living/Cadaveric			53 (82.8)/11 (17.2)
Living related			
Parent			12 (22.6)
Offspring			17 (32.0)
Sibling			21 (39.6)
Living unrelated			
Spouse			3 (5.67)
Bilirubin ( $\mu\text{mol/l}$ )	15.14 (10.7)	(3.61-31.1)	64
Creatinine ( $\mu\text{mol/l}$ )	59.6 (13.9)	(47-81)	64

**Table 3.** Postoperative complications and surgical data.

Variable	Mean (SD)	Median (range)	N (%)
Operation time (minute)	555 (114)	545 (330-830)	64
CIT (minute)	234.3 (153.4)	171.5 (60-630)	
Bleeding volume (ml)	1835.7 (1226.5)	1500 (600-8000)	
Postoperative complication			
Bleeding			18 (28.57%)
Biliary complications			21 (32.8%)
Bile leakage			9 (42.8%)
Biliary stricture (anastomotic)			8 (38%)
Biliary stricture (non-anastomotic)			1 (4.8%)
Cholangitis			3 (14.4%)
PVT			7 (10.93%)
Infection			18 (28.57%)
HAT			3 (4.68%)

CIT – cold ischemic time; HAT – hepatic artery thrombosis; PVT – portal vein thrombosis.

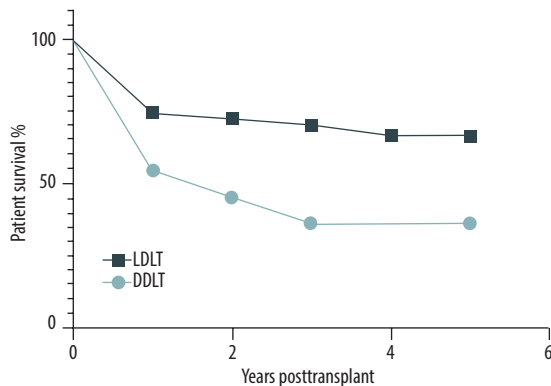
The mean age of transplant recipients was 44 years (range 15-63), with a slight majority of female recipients (53%) compared with male recipients (47%). The mean hospital stay was  $40 \pm 25$  days (range 11-196). Demographic and clinical characteristics of the liver recipients are shown in **Table 1**.

The mean age of liver donors was 31.5 years (range 19-54); 45 (70.35%) donors were men, and 19 (29.7%) were women. All living donors survived the procedure. Among living related donors, the donor was a parent of the recipient in 12 cases (22.6%), offspring in 17 cases (32.0%), and sibling in 21 cases (39.6%); the 3 unrelated living donors (5.67%) were the

spouse of the recipient. No major complications were experienced in living donors. Demographic and clinical characteristics of the liver donors are shown in **Table 2**.

The mean cold ischemic time was  $234.2 \pm 153$  min, ranging from 330 to 830 min. The mean operation time was  $555 \pm 114$  min. The mean bleeding volume was  $1835 \pm 1226$  mL, ranging from 600 to 8000 mL (**Table 3**).

Most of the recipients experienced biliary complications (n=21, 32.8%). Among these 21 cases, anastomotic biliary stricture occurred in 8 (38%), bile leakage in 9 (42.8%), nonanastomotic



**Figure 2.** Overall patient survival rate after living/deceased liver transplantation.

biliary stricture in 1 (4.8%), and cholangitis in 3 (14.4%). Bile leakage was treated conservatively in 3 cases (33.3%) and reoperation was performed in 5 cases (55.5%) to remove the biloma or reanastomosis. Anastomotic biliary stricture needed reoperation with Roux-en-Y hepaticojejunostomy. When high bilirubinemia persisted even after reanastomosis in recipients, percutaneous transhepatic draining of the bile ducts was performed. Portal vein thrombosis occurred in 7 recipients and hepatic artery thrombosis in 4 cases, all after LDLT.

Acute rejection was observed in 7 patients (10.9%) after liver transplantation, with 1 case (9%) occurring after DDLT and 6 cases (11.3%) after LDLT. There was a significant association between donor type (living/deceased) and rejection rate ( $P=0.004$ ) (Table 3). All patients with acute rejection were treated with steroid therapy. We did not observe any steroid-resistant rejection.

The overall patient survival rates for 1, 3, and 5 years were 75%, 69.5%, and 59.6%, respectively, for liver transplant recipient from a living donor and 54.5%, 45.5%, and 39% for a liver recipient from a deceased donor (Figure 2).

## Discussion

The National Research Oncology Center is one of the few transplant centers in Kazakhstan, the largest country of central Asia. In this study, we analyzed the outcome of 64 liver transplantations performed in our center since 2010. Clinico-demographic characteristics of donors, recipients, and outcomes were described in this paper. Our data showed that the main cause of ESLD among our patients was HBV, which accords with a systematic review indicating that Kazakhstan has the highest prevalence of HBV in central Asia [9]. Among a total of 64 liver transplantations, 53 recipients received a liver graft from

living donors. Worldwide, LDLT has developed significantly, with the highest distribution in Asian countries [10]. The main disadvantage of the living donation is the donor hepatectomy, which can lead to various complications [11]. We made a strict selection of so-called ideal donors; the volume of remnant liver varied from 35% to 40%, liver steatosis was less than 10%, and the mean age was 32.5 years. In our study, living donors did not experience any major complications.

The liver transplant procedure itself is technically complicated, and partial liver transplantation is an even more challenging procedure. Numerous perioperative complications occurred in our case series. Biliary and vascular complications are the major cause of morbidity and mortality after liver transplantation. The most common complication in our study involved biliary complications. The incidence of biliary complications in liver recipients varies from 10% to 15% in DDLT and from 15% to 30% in LDLT [12]. The rate of biliary complications in our study was 32.8%. Most of the cases of biliary stenosis were treated with reoperation and hepaticojejunostomy or transhepatic draining. Hepaticojejunostomy often led to chronic cholangitis and biliary cirrhosis of the liver graft.

Our data revealed that DDLT patients had fewer episodes of acute rejection (9% vs 11.3%), which is not similar to other transplant centers' data. We suggest that a higher rate of acute rejection in LDLT recipients might be due to a higher rate of hepatic artery thrombosis after LDLT.

Despite the high rate of acute rejection in LDLT patients, overall survival was significantly higher in LDLT recipients than in DDLT recipients ( $P<0.05$ ).

This study is limited due to the small-size cohort and its retrospective character. A longer observation period, a higher number of liver transplantation cases, and improved donor and recipient selection are necessary for further work.

## Conclusions

For developing countries, starting a liver transplant program is challenging due to many factors, such as insufficient financial support and lack of opportunity to train surgeons and other specialists. These factors are essential for the complicated procedure of liver transplantation and efficient follow-up. Improving surgical technique, preventing biliary and vascular complications, and overcoming the organ shortage problems remain to be achieved.

In conclusion, in Kazakhstan, similar to other developing countries, establishment of transplantation programs is essential for health care system improvement.

### Conflict of Interest

None.

### Acknowledgments

We would like to thank the transplant team of the National Research Oncology center for their great work throughout 10 years.

### References:

1. Murray KR, Carithers RL Jr. AASLD practice guidelines: Evaluation of the patient for liver transplantation. *Hepatology*. 2005;41:1407-32
2. Republican Center for Coordination of Transplantation (RCCT), Healthcare Ministry of Kazakhstan. Statistics. Waiting List. Accessed September 4, 2020. <https://transplant.kz/ru/> [in Russian]
3. Chen CL, Kabiling CS, Concejero AM. Why does living donor liver transplantation flourish in Asia? *Nat Rev Gastroenterol Hepatol*. 2013;10(12):746-51
4. Altinors N, Haberal M. Brain death and transplant in Islamic countries. *Exp Clin Transplant*. 2016;14(Suppl.3):48-52
5. Shaheen FAM, Souqiyeh MZ. How to improve organ donation in the MESOT countries *Ann Transplant*. 2004;9(1):19-21
6. Shaheen FAM, Souqiyeh MZ. Current obstacles to organ transplant in Middle Eastern countries. *Exp Clin Transplant*. 2015;13(Suppl.1):1-3
7. Abouna GM. Organ shortage crisis: Problems and possible solutions. *Transplant Proc*. 2008;40(1):34-38
8. Sultanaliev T, Zhexembayev A, Mukazhanov A, et al. Liver transplant outcomes in a newly started program. *Exp Clin Transplant*. 2015;13(Suppl.3):120-22
9. Davlidova S, Haley-Johnson Z, Nyhan K, et al. Prevalence of HIV, HCV and HBV in Central Asia and the Caucasus: A systematic review. *Int J Infect Dis*. 2021;104:510-25
10. Rela M, Reddy MS. Living donor liver transplant (LDLT) is the way forward in Asia. *Hepato Int*. 2017;11(2):148-51
11. Sun Z, Yu Z, Yu S, et al. Post-operative complications in living liver donors: A single-center experience in China. *PLoS One*. 2015;10(8):e0135557
12. Daniel K, Said A. Early biliary complications after liver transplantation. *Clin Liver Dis (Hoboken)*. 2017;10(3):63-67

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