Pregnancy After Liver Transplantation: Risks and Outcomes

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ABSTRACT

Objective. The aim of this study was to evaluate the outcomes of liver transplant recipients who became pregnant after transplantation.

Methods. The clinical data of all patients who underwent liver transplantation between January 2007 and December 2016 in our liver transplantation institute were reviewed. The following data were analyzed: indications for transplantation, recipient age at the beginning of pregnancy, the interval between transplantation and pregnancy, maternal and fetal complications, type of delivery, the health condition of neonates, and modifications in immunosuppressive therapy.

Results. During the study period, 1890 patients underwent liver transplantation. There were 185 women (9.8%) in childbearing age (15–45 years old), and 18 (9.7%) of them became pregnant during the study period. There were a total of 26 pregnancies. The mean age of patients at the time of operation was 25.3 ± 5.2 years, and the mean interval between operation and conception was 32.7 ± 15.3 months. Seventeen pregnancies (65.4%) ended in a live birth in the study. Six pregnancies (23%) resulted with no maternal or fetal complications. The most frequent maternal complication during pregnancy was pregnancy-induced hypertension (n = 3; 16.6%).

Conclusions. Despite advances in immunosuppressive therapy and increasing experience in the management of these patients, pregnancies in liver transplant recipients are still more risky than in the general population for both the mother and the fetus. Thus, the issues related to fertility should be comprehensively discussed with the patients and their partners, preferably before transplantation, and pregnancies in liver transplant recipients should be followed up more carefully by a multidisciplinary team.

LIVER transplantation (LT) continues to be the only effective treatment method for end-stage liver failure, which can affect people from all age groups, including women of childbearing age. Thus, there will be a group of women who want to become pregnant after transplantation. Furthermore, infertility often seen in women with end-stage liver disease is usually treated with transplantation, with the goal of restoring reproductive endocrine functions. In the United States, ~1000 women of childbearing age undergo LT each year [1].

The first successful pregnancy after LT was reported in 1978, ~15 years after the first successful LT [2]. Today, pregnancy is a relatively common occurrence after LT. Despite advances in immunosuppressive therapy and increasing experience in the management of these patients, pregnancies in LT recipients are still more risky than in the general population for both the mother and the fetus, and they need to be carefully followed up in specialized centers by a multidisciplinary team. These teams include an obstetrician experienced in high-risk pregnancies, a perinatologist, a transplant surgeon, and a transplant

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Table 1. Delivery Data of the Patients

Parameter	Value
Mean interval between operation and conception, mo	32.7 ± 15.3
Pregnancy outcomes (live birth/stillbirth/miscarriage)	17/3/6 (65.4%/11.5%/23.1%)
Mean gestational age at delivery in live births	37.4 ± 1.7
Mean birth weight in live births, g	3147 ± 658
Vaginal delivery/cesarean sections in live births	8/9 (47.1%/52.9%)

hepatologist [3]. Thus, issues related to fertility should be comprehensively discussed with the patients and their partners, preferably before transplantation, and the timing of pregnancy should be well planned.

The most frequently reported complications in the fertile, prenatal, and postnatal periods of the pregnant LT recipient include anemia, pregnancy-induced hypertension (PIH), preeclampsia, intrauterine infections, cholestasis, pyelonephritis, congenital cytomegalovirus infection, perinatal infection with hepatitis B virus (HBV) and hepatitis C virus, prematurity (~40%), prenatal infections, intrauterine growth restriction (~20%), birth defects, and immune suppression [1,3–5].

The aim of the present study was to evaluate the outcomes of LT recipients who became pregnant after transplantation.

PATIENTS AND METHODS

Clinical data of all patients who underwent LT between January 2007 and December 2016 in our LT institute were reviewed. Data were obtained from a prospectively maintained database. Data of the patients who became pregnant during the follow-up period after LT were analyzed. The following data were analyzed: indications for transplantation, recipient age at the beginning of pregnancy, the interval between transplantation and pregnancy, maternal and fetal complications, type of delivery, the health condition of neonates, and modifications in immunosuppressive therapy.

All data management and statistical analyses were performed by using IBM SPSS version 20.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, United States). Means are reported with standard deviations. Continuous variables were compared with Student *t* tests or Mann-Whitney tests (for nonnormal data), and categorical data were compared with χ^2 tests.

RESULTS

Patients

A total of 1890 patients underwent LT during the study period. There were 185 women (9.8%) in childbearing age (15–45 years old), and 18 of them (9.7%) became pregnant during the study period. Six patients (2.7%) had multiple pregnancies (2 in 4 patients, 3 in 2 patients), and there were a total of 26 pregnancies. All of the 18 patients received an adult-to-adult living donor LT in our study. The mean age of the patients at the time of operation was 25.3 ± 5.2 years (range, 21–35 years), and the mean interval between operation and conception was 32.7 ± 15.3 months (range, 7–76 months).

Indications for LT

The etiology of end-stage liver disease was as follows in these study patients: HBV in 8 patients (44.4%), Budd-Chiari syndrome (BCS) in 4 patients (22.2%), hepatocellular carcinoma (HCC) in 2 patients (11.1%), cryptogenic chronic hepatitis in 2 patients (11.1%), fulminant hepatitis A in 1 patient (5.6%), and α_1-antitrypsin deficiency in 1 patient (5.6%).

Delivery Outcomes

Seventeen pregnancies (65.4%) ended in a live birth in this study. In the live births, the mean gestational age at delivery was 37.4 ± 1.7 weeks (range, 32–40 weeks), and there were 6 (35.3%) preterm deliveries. The mean birth weight was 3147 ± 658 g (range, 2200–4800). Four neonates (25%) were born at low birth weight. Cesarean sections were performed in 9 deliveries (52.9%). There were no differences in obstetric outcomes in terms of delivery methods (Table 1).

Miscarriage and stillbirth occurred in 6 (23.1%) and 3 (11.5%) pregnancies, respectively. The miscarriages and stillbirths occurred at a mean of 10.2 ± 2.8 weeks and 31.3 ± 4.1 weeks. No congenital abnormalities were diagnosed in this study.

Maternal Complications

Tacrolimus was the preferred immunosuppressive drug in all patients during the study period. Dosage adjustments of tacrolimus were required in 5 patients (27.8%) during pregnancy. Mycophenolate mofetil was additionally used in 1 patient (11.1%).

Maternal complications during pregnancy were as follows: PIH in 3 patients (16.6%), preeclampsia in 2 patients (11.1%), gestational diabetes mellitus in 2 patients (11.1%), thrombocytopenia in 2 patients (11.1%), various infections in 2 patients (11.1), viral reactivation in 1 patient (11.1% of patients with HBV), chronic rejection in 1 patient (11.1%), and recurrence of HCC in 1 patient (50% of HCC patients) (Table 2).

Table 2. Maternal Complications

Complication	No. (%)
No complication	6 (23)
Hypertension	3 (16.6)
Preeclampsia	2 (11.1)
Gestational diabetes mellitus	2 (11.1)
Thrombocytopenia	2 (11.1)
Infections	2 (11.1)
Viral reactivation	1 (11.1 of patients with HBV)
HCC recurrence	1 (50 of patients with HCC)

Abbreviations: HBV, hepatitis B virus; HCC, hepatocellular carcinoma.