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## Case Report

# Second successful pregnancy following liver transplantation

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### ABSTRACT

Liver transplantation for end stage liver disease, offers the recipient a near normal life, including pregnancies for women. Successful pregnancies have been reported, but successful second pregnancies are rare. We present our patient with a second successful pregnancy following her liver transplantation. A 22-year-old living donor liver transplant (LT) recipient was enrolled in our unit for antenatal care of her second pregnancy. Her native liver had failed due to autoimmune hepatitis. She had her first planned pregnancy at 19 months post-transplant. The second pregnancy was a spontaneous conception a year later. The obstetric parameters were normal, but she developed signs of suspected graft rejection and hence an emergency cesarean section was done. A preterm baby was delivered with a good APGAR score. The baby was treated in neonatal intensive unit for four days. The mother recovered well and the liver parameters normalized on the sixth postoperative day. Liver transplantation restores fertility in transplant recipients. Pregnancy, the liver graft and the associated medications have a complex interplay. Post LT pregnancy outcome can be optimized with a multidisciplinary approach. Better understanding and close monitoring is essential for a successful outcome.

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## 1. Case Report

A 22-year-old living donor liver transplant(LT) recipient was enrolled in our unit for antenatal care. She had undergone successful liver transplantation for end stage liver disease due to autoimmune hepatitis in 2016, at the age of twenty. Post liver transplantation, she was on triple immunosuppression viz tacrolimus, glucocorticoids and mycophenolate mofetil (MMF) along with thyroxine replacement for autoimmune hypothyroidism. With a stable allograft function, MMF was discontinued a year after LT. She had her first planned pregnancy at 19 months post-transplant. She delivered a healthy baby weighing 3.5 kg at 36 weeks of gestation by LSCS for an obstetric indication. Neonatal period and developmental

milestones were normal. She continued breastfeeding with close monitoring of allograft function. Post lactation she had regular menstruation. Her liver function tests (LFT) continued to be normal. Second pregnancy was a spontaneous conception a year later, with normal obstetric parameters. Her initial blood parameters including liver function tests were within normal range except for a low hemoglobin. She received multidisciplinary team care consisting of the obstetrician, hepatologist, endocrinologist and later a neonatologist. She was on Tacrolimus with regular monitoring for dose titration. At 32 weeks of gestation, she presented with significant fatigue. She had no jaundice, fever or signs of liver failure. However, there was elevation of liver enzymes ALT, AST and GGT (5 x UNL). Ultrasound examination showed mild increase in hepatic echogenicity with patent vasculature and a non-obstructed biliary system. The fetus was viable.

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Viral (Hepatitis A, B, C, E and HSV) and vasculitic etiology were excluded. Acute cellular rejection was the most likely etiology. She was treated with tacrolimus and intravenous methylprednisolone. Emergency caesarean section was done to prevent further deterioration. A preterm baby weighing 2.9kg was delivered with a good APGAR score. The baby received treatment in the NICU for four days. The mother recovered well and the LFT became normal on the sixth postoperative day. She was treated with routine antibiotics, analgesics and thromboprophylaxis.

## 2. Discussion

Liver transplantation is the only curative option for end stage liver disease. It optimizes quality of life with return of fertility and other endocrine functions.<sup>1</sup> Common causes for liver failure requiring transplant in the reproductive group are autoimmune hepatitis, Wilson disease, Budd-Chiari syndrome and viral hepatitis.<sup>2</sup> Since liver plays a major role in sex hormone metabolism, normal functioning of the liver restores the Hypothalamic-Pituitary-Ovarian axis with return of fertility. However, the optimal time for conception is considered as 12-24 months following transplant.<sup>3</sup> This allows time for optimal recovery, development of immune tolerance and minimizes risk of cellular rejection. Adequate contraception during the first-year post LT is mandatory.

Our patient with post LT pregnancy had a favorable outcome with preserved allograft function in the first pregnancy in the second year following LT. However, the second pregnancy encountered mild acute cellular rejection. The transplant to pregnancy duration was three years for the second planned pregnancy. The prevalence of acute cellular rejection ranges from 0-17% in post LT recipients in multiple studies.<sup>3</sup> The risks to the graft during the pregnancy are graft dysfunction and recurrence of the primary disease. The risk factors for the pregnancy are maternal age, renal insufficiency and interval from transplantation.<sup>3</sup> Physiological volume expansion, third space and adipose tissue redistribution related to the pregnancy can influence the drug concentration. Hence, regular close monitoring of immunosuppression is mandatory. The estrogen surge in the third trimester also has a cholestatic effect on hepatocytes accelerating the graft dysfunction. The physiological effect of pregnancy predisposes the transplanted liver for adverse events such as cholestatic liver injury, acute cellular rejection, thrombotic vascular injury and de-novo autoimmune induction. Pregnancy, immunosuppression and medications can interact adversely with each other, potentially affecting the baby as well as the liver graft.<sup>4</sup> Understanding these interactive effects is important in managing these patients.

Planned conception, regular monitoring of LFT and immunosuppression during pregnancy help to avoid morbidities. Glycemic monitoring, timely treatment of opportunistic infections especially vulvovaginal infections,

treatment of associated endocrinopathies and close fetal monitoring are important for a favorable outcome.

Among the immunosuppressants tacrolimus, cyclosporine and glucocorticoids have good safety profiles except mycophenolate mofetil which needs to be discontinued during pregnancy due to significant teratogenicity.<sup>5</sup> Hence, the role of planned pregnancy, contraception and the safety profile of immunosuppressants need to be counseled to recipients. Thromboprophylaxis needs to be continued when the original indication for transplant is Budd-Chiari Syndrome. However, warfarin needs to be changed to heparin as early as possible. The timing and mode of delivery is dependent on clinical situations and obstetric indications. Possible maternal complications are graft rejection, diabetes, hypertensive disorders, renal failure, antepartum and postpartum hemorrhage and venous thromboembolism.<sup>4</sup> Perinatal outcome is affected by prematurity, intrauterine growth restriction, congenital malformations and infections. A live birth rate of 69% to 73%, 31% incidence of prematurity and a low-birth-weight incidence of 29% has been reported.<sup>4,6</sup> Breastfeeding is not contraindicated in post LT recipients on immunosuppression.

## 3. Conclusion

Liver transplantation restores the fertility in transplant recipients. Post LT pregnancy outcome can be optimized with a multidisciplinary approach. Pregnancy, the liver graft and the associated medications have a complex interplay. Better understanding and close monitoring is essential for a successful outcome.

## 4. Source of Funding

None.

## 5. Conflict of Interest


None.

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