

## 1-MINUTE CONSULT

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# Q: A female liver transplant recipient asks: Can I become pregnant?

**A:** Yes, pregnancy is possible, but not immediately after transplant, and it involves risks. Appropriate management and multidisciplinary care are necessary to optimize the outcomes.

## ■ HOW LONG SHOULD PREGNANCY BE POSTPONED?

Hypogonadism and amenorrhea are common and multifactorial in women with end-stage liver disease. Hypogonadotrophic hypogonadism, elevated estrogen level, and malnutrition all contribute to the problem.<sup>1</sup> However, most premenopausal women experience a return of their menstrual cycle, and possibly of fertility, within the first 10 months after liver transplant,<sup>2,3</sup> after which pregnancy is possible.

In transplant recipients of childbearing age, the need for preconception counseling and family planning should be emphasized. The timing, potential risks, and outcomes of pregnancy, and the importance of coordinated prenatal and perinatal care should be addressed.<sup>4</sup> The National Transplant Pregnancy Registry guidelines recommend postponing conception until:

- At least 1 year has elapsed after transplant
- Graft function is stable
- Medical comorbidities such as diabetes and hypertension are well controlled
- Immunosuppression is at a low maintenance level.<sup>3</sup>

Strong evidence suggests that an appropriate liver transplant-conception interval reduces adverse maternal and fetal outcomes. In particular, the risks of a low birth weight, graft rejection, and loss during pregnancy are significantly decreased.<sup>3</sup> Therefore, contracep-

tion must be initiated after transplant before any sexual activity, with no preference as to the form of protection used.

Limited data demonstrate the safety and efficacy of combined oral contraceptives and transdermal contraceptive patches in stable solid-organ recipients.<sup>5,6</sup> Estrogen-containing contraceptives should, however, be avoided in recurrent liver disease after transplant because of the risk of increased hepatic toxicity.

## ■ MANAGING RISKS ASSOCIATED WITH PREGNANCY

Physicians should be alert to the possibility of a pregnancy. Early diagnosis allows the optimization of management and outcomes, as complications are increased in this population of expectant mothers.<sup>7</sup>

Well-known risks to the expectant liver transplant recipient include hypertension and preeclampsia.<sup>8</sup> Moreover, infants born to these patients have a higher risk of prematurity and low birth weight.<sup>3,7,9</sup> However, rates of neonatal or maternal deaths and birth defects do not differ significantly from those seen in the general population. Graft rejection is a potential complication, with rates varying between 0% and 20% in different studies.<sup>3</sup>

Multidisciplinary care is therefore crucial during these high-risk pregnancies.<sup>10</sup> An obstetrician, a hepatologist, and a perinatologist should collaborate to maximize outcomes.<sup>11</sup> Frequent evaluations, preferably 2 weeks apart, are suggested for the serial assessment of fetal growth.

Furthermore, daily monitoring of the blood pressure and aggressive management of hypertension are recommended. Methyldopa appears to be the drug treatment of choice.<sup>12</sup>

**Preconception counseling and family planning should be emphasized**

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Close monitoring of graft function and liver biopsy in suspected graft rejection are of essence as well.<sup>3</sup> Routine screening for urinary tract infection, cytomegalovirus and toxoplasmosis infections, gestational diabetes, and pre-eclampsia should also be undertaken.

## MANAGING IMMUNOSUPPRESSION IN THE PREGNANT PATIENT

The choice of immunosuppression is ideally made before pregnancy. All immunosuppressive drugs cross the placenta. Thus, in theory, all agents carry risks of teratogenicity and fetal loss. However, immunosuppression is crucial in avoiding rejection. Furthermore, the use of appropriate immunosuppressive regimens prevents negative outcomes. Drugs are classified as class A (safest to use in pregnancy), through classes B, C, D, and X.

Tacrolimus (class C) monotherapy appears

to be safe, with attention to the maintenance of therapeutic levels throughout pregnancy. Allograft function and tacrolimus serum levels need to be monitored because of the change in the volume of drug distribution. Cyclosporine (a pregnancy class C drug), prednisone (class B), and azathioprine (class D) are also reasonable options and may also be used if judged necessary.<sup>13</sup>

Mycophenolic acid and mTOR (mammalian target of rapamycin) inhibitors such as sirolimus and everolimus are significantly teratogenic and should be avoided in pregnant women. They are more commonly associated with spontaneous abortion, structural abnormalities, and birth defects than other immunosuppressive drugs, especially if taken in the early stages of pregnancy. Cleft lip and palate, absent auditory canals, and microtia have been reported.<sup>2,13</sup>

## REFERENCES

1. Bell H, Raknerud N, Falch JA, Haug E. Inappropriately low levels of gonadotrophins in amenorrhoeic women with alcoholic and non-alcoholic cirrhosis. *Eur J Endocrinol* 1995; 132:444–449.
2. Mass K, Quint EH, Punch MR, Merion RM. Gynecological and reproductive function after liver transplantation. *Transplantation* 1996; 62:476–479.
3. Coscia LA, Constantinescu S, Moritz MJ, et al. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. *Clin Transpl* 2009; 103–122.
4. Parolin MB, Coelho JC, Urbanetz AA, Pampuch M. Contraception and pregnancy after liver transplantation: an update overview. *Arq Gastroenterol* 2009; 46:154–158. In Portuguese.
5. Paulen ME, Folger SG, Curtis KM, Jamieson DJ. Contraceptive use among solid organ transplant patients: a systematic review. *Contraception* 2010; 82:102–112.
6. Jabiry-Zieniewicz Z, Bobrowska K, Kaminski P, Wielgos M, Zieniewicz K, Krawczyk M. Low-dose hormonal contraception after liver transplantation. *Transplant Proc* 2007; 39:1530–1532.
7. Coffin CS, Shaheen AA, Burak KW, Myers RP. Pregnancy outcomes among liver transplant recipients in the United States: a nationwide case-control analysis. *Liver Transpl* 2010; 16:56–63.
8. Heneghan MA, Selzner M, Yoshida EM, Mullhaupt B. Pregnancy and sexual function in liver transplantation. *J Hepatol* 2008; 49:507–519.
9. Ho JK, Ko HH, Schaeffer DF, et al. Sexual health after orthotopic liver transplantation. *Liver Transpl* 2006; 12:1478–1484.
10. Jabiry-Zieniewicz Z, Dabrowski FA, Pietrzak B, Wielgos M. Pregnancy complications after liver transplantation. *Int J Gynaecol Obstet* 2015; 128:27–29.
11. Parhar KS, Gibson PS, Coffin CS. Pregnancy following liver transplantation: review of outcomes and recommendations for management. *Can J Gastroenterol* 2012; 26:621–626.
12. McKay DB, Josephson MA, Armenti VT, et al; Women's Health Committee of the American Society of Transplantation. Reproduction and transplantation: report on the AST Consensus Conference on Reproductive Issues and Transplantation. *Am J Transplant* 2005; 5:1592–1599.
13. Sifontis NM, Coscia LA, Constantinescu S, Lavelanet AF, Moritz MJ, Armenti VT. Pregnancy outcomes in solid organ transplant recipients with exposure to mycophenolate mofetil or sirolimus. *Transplantation* 2006; 82:1698–1702.

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**Guidelines  
recommend  
waiting at least  
1 year  
after transplant  
before  
pregnancy**