# Pregnancy in Renal Transplant Recipients

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**Fertility in women with kidney failure is restored by transplantation. It requires careful planning and is only advisable in women with good kidney function, controlled blood pressure, and general good health. Immunosuppressive drugs carry risks for the fetus, but the risks of prednisone, azathioprine, cyclosporine, and tacrolimus are surprisingly low. Mycophenolate is teratogenic. The success rate for pregnancy in kidney transplant recipients is lower than in the general population with 70% to 80% of pregnancies resulting in surviving infants. Prematurity, intrauterine growth restriction, and preeclampsia are all increased. Complications are higher and outcomes are worse for women with serum creatinine levels over 1.3 mg/dL. Ten to 15% of women have a temporary or permanent decline in kidney function, particularly if prepregnancy creatinine is high. Transplant-related infections can be serious for the mother and fetus. A multidisciplinary team should coordinate care.**

**Key Words:** Pregnancy, Kidney transplant, Immunosuppressive drugs, Opportunistic infection

On March 10, 1958, the first woman to receive a kidney transplant gave birth to the first baby born to a kidney transplant recipient.[1] She was transplanted from an identical twin sister, thereby avoiding the problems of immunosuppressive drugs and associated infections in pregnancy. However, this event led to a few important new observations. Transplantation restored fertility in women with kidney failure. The function of a solitary kidney was sufficient to sustain pregnancy. The proximity of the uterus to the transplanted kidney did not cause mechanical problems.

The potential for pregnancy raised a multitude of questions about the effect of pregnancy on the transplanted kidney and the effect of kidney disease on the fetus and on pregnancy-related complications. The kidney transplant recipients whose pregnancies followed this first woman were treated with immunosuppressive drugs, with each new generation of drugs requiring evaluation for teratogenicity. All immunosuppressive drugs put the women at risk for opportunistic infections that can be devastating for the developing fetus.

## Fertility in Transplant Recipients

Women treated with dialysis have markedly decreased fertility (see "Changes in Fertility and Hormone Replacement Therapy in Kidney Disease" in this issue); however, kidney transplantation is usually accompanied by a return of fertility. Even women who have follicle stimulating hormone and luteinizing hormone levels in the postmenopausal range may have normalization of levels and restoration of fertility. The return of fertility is not universal. Pietrzak and colleagues[2] noted that only 68.1% of 63 kidney transplant recipients had regular menstrual cycles whereas the rest had irregular cycles. Ovulation was documented by rising progesterone and ultrasound visualization of follicle growth in 59.5% of women with regular menstrual cycles.

In vitro fertilization was used in 17 of 1134 pregnancies reported to the National Transplant Pregnancy Registry (NTPR), 11 in recipients of kidney transplants.[3] It is not clear whether infertility is more common in kidney transplant recipients than in the general population. Sirolimus is known to decrease sperm counts and fertility in men,[4] but its effect in women is unknown.

## Counseling

The discussion about pregnancy and childbearing should begin when a woman of childbearing age is seen for her first pretransplant evaluation and continued after transplantation. For those who are too young to be considering pregnancy, the matter should still be mentioned and discussed again as the patient gets older. Part of counseling includes emphasis on the need to continue immunosuppressive therapy. Without the explicit knowledge that loss of graft function carries a higher risk for the baby than the medications, some women have elected to stop drugs on their own for fear of an adverse effect on the baby. Counseling should also emphasize the need to plan pregnancies because medications often need to be changed before conception. Every woman treated with mycophenolate products should be advised of and reminded of their teratogenic potential. Fully 26% of 440 pregnancies reported in an early survey in 1979 ended in elective abortion, often because pregnancy was unexpected and viewed as dangerous.[5]

It is usually advised that a woman wait at least 1 year before attempting conception. Many would prefer a wait of 2 years but recognize that after a long wait for transplant, the window of fertility may be narrow. The

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*Conflict of Interest: S.H. owns stock in Amgen and talks about using erythropoietin in pregnancy.*

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guidelines that are used for advising transplant recipients about pregnancy are listed in Table 1.

## Outcome of Pregnancy in Kidney Transplant Recipients

The NTPR is the largest body of information on pregnancy outcomes in transplant recipients. Over its 20-year history, the registry has collected data on 1490 pregnancies (1525 outcomes) in 922 kidney transplant recipients. Among the 666 women treated with calcineurin inhibitors (CNIs), 73.8% of the 1026 pregnancies (1066 outcomes) resulted in live births.[3] There were 12 neonatal deaths (1.1%). Other outcomes included 17.3% spontaneous abortions, 4.5% therapeutic abortions, 2.5% were stillborn, and 0.6% were ectopic pregnancies.[3] Other series report similar results.[6-9] In one recent report, only 32 of 53 (60%) pregnancies in kidney transplant recipients resulted in surviving infants, 69.5% if elective terminations are excluded.[7]

Pregnancy in transplant recipients is also associated with a high rate of prematurity and intrauterine growth restriction. Of the NTPR pregnancies discussed above, 52% resulted in delivery before 37 weeks gestation.[3] The frequency of prematurity has remained fairly constant over time. The severe prematurity that we see in pregnant dialysis patients is less common.

**CLINICAL SUMMARY**

- Fertility is restored in kidney transplant recipients.
- Successful pregnancy is likely in a woman with good kidney function and controlled blood pressure when undertaken more than a year after transplant.
- Immunosuppressive drugs need to be modified for pregnancy.
- Patients need close monitoring for changes in kidney function and infection.

## Effect of Pregnancy on Graft Function

In 1985, Davison published a report on prospectively studied kidney graft function during 10 pregnancies in 8 kidney transplant recipients.[10] All had creatinine clearances of greater than 50 cc/min, less than 250 mg/24 hours of protein, and well controlled blood pressure. There was a mean increase in creatinine clearance of 30% by weeks 9 to 12 (range 10%-60%) despite compensatory hypertrophy and increased function of the solitary kidney at the time of transplant. In 2 patients kidney function was lower than prepregnancy levels postpartum. Less is known about changes in glomerular filtration rate in women with impaired kidney function and in women who conceived in the era of CNIs.

There are several studies with case controls looking at the outcome of pregnancy on kidney graft function. First and colleagues reported graft function in 18 women who underwent 25 pregnancies compared with 26 female controls and 23 male controls.[11] Mean follow-up for the group who became pregnant was 11.8 years after transplantation and 6.9 years after pregnancy with similar periods of follow-up for the control groups. At last follow-up, graft survival was 77.8% in women who had become pregnant, 69.2% in the female controls, and 69.8% in the male controls (not significant). Twenty-eight percent of pregnant women and 31% and 22% of the 2 control groups used cyclosporine A (CsA). A case-control report from the European Dialysis and Transplant Association including 53 women who became pregnant matched with controls for year of transplant, type of transplant, and serum creatinine found kidney function unchanged in case and controls in 67% and worse in both in 9%.[12] In 15% of pairs, the control had a deterioration of kidney function and in 9% the patient who became pregnant had a worsening of kidney function. Sturgiss and Davison compared a group of 18 high-risk women who had 34 pregnancies to a control group matched for factors that affected kidney transplant longevity and found no effect of pregnancy on graft survival.[13] All of these series are limited by the inclusion of only a few women with impaired kidney function and either a small or unspecified number of women treated with CsA. There is a single controlled study that suggests that graft function is adversely affected by pregnancy. Salmela and colleagues reported long-term graft function in 22 female kidney transplant recipients with 29 pregnancies compared with 38 female controls matched for cause of kidney failure, kidney source, immunosuppression, time from transplant, and serum creatinine.[14] CsA was used during 9 pregnancies and 4 had a prepregnancy serum creatinine of greater than 1.48 mg/dL. During the follow-up period, 8 of the women who became pregnant lost their grafts, 1 at 1 month postpartum. The other grafts were lost between 1 and 11 years postpartum, but in 3 the deterioration of graft function began during pregnancy. At the 10-year follow-up, transplant survival was 100% for the control group and 69% for the group who had pregnancies ($P < .005$). Graft loss could not be correlated with elevated serum creatinine at the time of conception. The difficulty generalizing from this study lies in the rarity of centers with a 10-year kidney transplant survival of 100% such as was seen in the control group. The bulk of the evidence suggests that graft function is usually not adversely affected by pregnancy in women with serum creatinine less than 1.5 mg/dL treated with prednisone and azathioprine.

The long-term effect of pregnancy on kidney transplant function is most influenced by prepregnancy kidney function. A woman who becomes pregnant with a serum creatinine of 1.4 mg/dL or less is unlikely to