



Successful Pregnancy and Delivery with Good Maternal and Fetal Outcome in a Kidney Transplant Recipient

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ABSTRACT

Conception and successful completion of pregnancy is rare in women with end-stage kidney disease. Given the rising burden of chronic kidney disease, it is quite common to see more women in their childbearing ages being diagnosed with the condition. As the kidney disease progresses, fertility chances reduce and pregnancy becomes a rarity. In addition to dealing with dialysis and its consequences, the women with end-stage kidney disease also face the trauma of infertility and inability to start their families. At such times, pregnancy and delivery following successful kidney transplantation with return of normal kidney function, offers a ray of hope to women of childbearing ages. We report the case of a young woman with end-stage renal/kidney disease (ESRD) on hemodialysis for 2 years, who underwent cadaveric kidney transplantation with subsequent excellent allograft function. Two years post-transplantation, she went ahead with a successful pregnancy and delivery of a normal birth weight baby, and preserved renal allograft function.

Keywords: Kidney transplant recipient, Maternal outcomes, Pregnancy.

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INTRODUCTION

Case History

A 25-year-old married woman was seen in gynecology clinic for evaluation of infertility in 2010. She denied any symptoms other than an occasional headache, anorexia and weakness. Preliminary blood tests showed markedly abnormal renal parameters with blood urea nitrogen

(BUN) of 60 and serum creatinine of 6.5. She was referred to Nephrology. She had no prior history of hypertension, diabetes, hepatitis or nephrolithiasis. She denied any specific urinary symptoms. Family history was non-contributory and she was not taking non-steroidal anti-inflammatory drugs or any herbal supplements. Upon physical examination, significant findings were pallor and hypertension. A sonography of the kidneys revealed bilateral, small and shrunken kidneys with increased cortical echogenicity without any hydronephrosis or calculi. Urine analysis showed proteinuria without any casts or crystals. The 24 hours urine sample showed 1.2 gm of proteinuria. In addition to the raised BUN and serum creatinine, other complications of renal dysfunction, like anemia, metabolic acidosis and elevated potassium were also noted. A diagnosis of end-stage renal disease (ESRD) was made and further treatment options were discussed. She was started on antihypertensive medications, sodium bicarbonate tablets, and phosphorus binder tablets. Iron and erythropoietin injections were added. Given the absence of any reversible causes of renal dysfunction and the small sized shrunken kidneys seen on sonography, renal replacement therapy options were considered. Kidney transplant options were discussed with the patient and her family. Her blood group was O⁺. Given no potential living donors in the family, she was placed on a cadaver transplant wait list with zonal transplant co-ordination centre and MGM New Bombay Hospital, Vashi. A left arm arteriovenous fistula was placed, and hemodialysis treatments started twice a week for azotemia and uremic symptoms.

After being on hemodialysis for nearly a year and a half, she received a call from MGM New Bombay Hospital, Vashi, regarding the availability of a blood group-matched cadaver donor. She underwent a cadaveric kidney transplant surgery in June 2012. The donor was a 19-year-old, blood group O⁺ female, declared brainstem dead following a road traffic injury. The transplanted kidney functioned well with good urine output and steady decline in serum creatinine values. Her immunosuppressive medicines included tacrolimus, mycophenolate mofetil and prednisolone. Post-discharge, she continued with regular follow-up and the renal allograft function was excellent with a baseline serum creatinine of 0.7 to 0.8. She had mild hypertension, which was treated with metoprolol.

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She expressed her desire to start a family, but was advised to wait for at least a year post-transplant and continue with contraception in the interim. After about 2 years, given excellent allograft function with no episodes of rejection or infections, she was permitted to try for pregnancy. For planning a pregnancy, her immunosuppressive medications were changed; mycophenolate mofetil was discontinued and azathioprine was started. Prednisolone and tacrolimus were continued. Metoprolol was switched to labetalol. The high-risk nature of the pregnancy was explained to the family along with the need to closely monitor the patient during the pregnancy; especially to monitor kidney graft function, infection, rejection or development of pre-eclampsia.

She conceived in March, 2014. During pregnancy, she was closely followed-up both by a obstetrician and a nephrologist. Blood pressure and renal function were monitored regularly. Pregnancy course was uneventful with no infections, graft rejection or pre-eclampsia. Transplant kidney function remained stable. In the third trimester, she developed gestational diabetes that responded well to diet control and reduction in tacrolimus dose. Blood pressures were elevated, requiring increases in the labetalol doses. In the 35th week of pregnancy, she was taken up for cesarean section, given worsening blood pressure (BP) though no proteinuria. Stress dose steroids were given intraoperatively. She delivered a healthy 2.5 kg weight baby in December, 2014.

Post-pregnancy, her renal allograft function remains stable. Breast feeding has been deferred given need to continue immunosuppressive medicines that get excreted in the milk. Her kidney function remains stable with a serum creatinine of 0.7. She has been switched back to mycophenolate mofetil from azathioprine. Both mother and baby are doing well.

DISCUSSION

Kidney disease is associated with a risk of both maternal and fetal adverse outcomes. Pregnancy in a woman with kidney disease can increase the risks for gestational hypertension, pre-eclampsia and eclampsia. Pregnancy confers a serious risk of worsening of kidney function during pregnancy in women with pre-existing moderate to severe chronic kidney disease (defined as serum creatinine > 1.3 mg/dl and > 1.9 mg/dl respectively).¹ Fetal risks include intrauterine growth retardation, preterm birth and still birth.

Pregnancy in end-stage kidney disease (ESRD) population is uncommon.² Infertility rates are high in them, and according to a study; the reported frequency of conception in women on dialysis is around 0.3 to 1.5% per year.³ Rate of fetal deaths during pregnancies

in dialysis patients is significantly high although more recent data suggest improved outcomes with higher rates of live births (40–86% of all pregnancies).^{4,5} The improved pregnancy outcomes in women with ESRD on dialysis is thought to be due to an aggressive management of uremia with intensified dialysis keeping target blood urea levels lower than 50 mg/dl (recommended measures include dialysis more than 36 hours per week, long nocturnal dialysis and more frequent dialysis 4 to 6 times/week, etc). Additional suggested measures include correction of metabolic acidosis and hypocalcemia, targeting hemoglobin between 10 and 11 g/dl with erythropoietin injections, avoidance of hypotension during dialysis and careful monitoring of nutrition and adequate protein intake by the mother. These measures are intended to provide the best possible environment to the developing fetus to ameliorate polyhydramnios, improve maternal blood pressure and increase the gestational age and fetal birth weight.⁵⁻⁷ However, despite these improved fetal outcomes, pregnancy in women on dialysis poses a significant risk of severe hypertension, pre-eclampsia and premature delivery.⁸ Under such circumstances, if a kidney transplant option is feasible, it would be the ideal situation for women of childbearing age with ESRD, to plan for pregnancy after successful kidney transplantation.

Post-transplantation, fertility is restored. However, the rate of successful continuation of pregnancy to term is still quite low as compared to the general population. According to a study, 55% of pregnancies in transplant recipients resulted in a live birth, as compared to nearly 70% in the general population.⁹ In addition, the frequency of pre-eclampsia, intrauterine growth retardation and premature delivery are increased in transplant recipients.⁹⁻¹³

Traditionally, women were usually advised to wait at least two years after transplantation so as to avoid complications arising from immunotherapy and rejection.¹⁴ However, longer wait times for a kidney transplant and increasing age of women pose reduced time for successful pregnancy post-transplantation for such women of childbearing age. According to American society of transplantation, consensus opinion, as long as graft function is optimal (defined as serum creatinine < 1.5 mg/dl, with < 500 mg/24 hours protein excretion), no use of teratogenic medications, and immunosuppressive medicines at stable levels, the patient can safely proceed with the pregnancy.^{11,15} As in the case of chronic kidney disease, pregnancy has little or no effect on the kidney allograft function, provided that the allograft is functioning well at baseline. Hence, it is recommended that prior to contemplating pregnancy in a transplant recipient, the serum creatinine level should be stable and < 1.5 mg/dl, and urinary protein excretion < 500 mg/day.¹¹

Specific maternal concerns in pregnant renal transplant women are—onset of hypertension, worsening of pre-existing hypertension, development of proteinuria and pre-eclampsia, renal allograft rejections, superimposed infections (especially urinary tract infections), and development of gestational diabetes.

Prevalence of hypertension is high among pregnant renal transplant women, up to 73% according to registry report.¹⁶ In addition, renal transplant patients with hypertension are at higher risk for development of superimposed pre-eclampsia with an incidence of 15 to 25% as compared to 5% of normotensive pregnancies.¹⁷ Hence, close monitoring of blood pressure and use of approved antihypertensive medications during pregnancy for BP control is mandatory in the management of pregnant renal transplant recipient.

Renal allograft rejection is another risk during pregnancy, especially because changes in blood volume can alter serum levels of immunosuppressive medications. Thus, immunosuppressive drug levels are checked frequently during pregnancy for dose titration.^{11,18-20} A transplant renal biopsy can be undertaken during pregnancy, if there are concerns of rejection and appropriate treatment can be started.

Pregnant renal transplant women are at higher risk for developing gestational diabetes, hence, screening glucose tolerance test is recommended each trimester.²¹ Among infections, urinary tract infections are seen more frequently in pregnant renal transplant recipients.²² Hence, screening and treatment of asymptomatic bacteriuria is also recommended.

Specific concerns to the fetus in pregnancies post-renal transplantation include—preterm delivery, low birth weight and intrauterine growth retardation.^{18,21} Thus, serial sonographic surveillance of the fetus is carried out during such pregnancies.²¹ In addition, effect of immunosuppressive medications on the developing fetus is a major concern. Among the immunosuppressive medicines, mycophenolate mofetil in particular has been associated with structural malformations in the fetus and its use is contraindicated in pregnancy.²³ Mycophenolate should be discontinued at least 6 weeks prior to planning pregnancy. Azathioprine is safer and can be used as a substitute to mycophenolate mofetil during pregnancy. Calcineurin-inhibitors like tacrolimus and cyclosporine are used during pregnancy, although their levels should be closely monitored and doses adjusted to avoid toxicity as well as maintain adequate immunosuppression during pregnancy.^{11,20}

Breastfeeding is generally deferred in kidney transplant recipients due to the immunosuppressive medications being secreted in breast milk and risk of exposure to the baby. However, due to lack of data and controlled

studies on the pharmacokinetics and levels of immunosuppressive medications in breast milk, there is no expert consensus that absolutely contraindicates breast feeding in women on immunosuppressive medications.^{11,15}

CONCLUSION

A successful kidney transplant offers an opportunity to young women with advanced kidney disease to contemplate pregnancy and delivery. Although lower than the general population, the successful maternal and fetal outcomes post-pregnancy in a kidney transplant recipient certainly gives them a ray of hope. Such pregnancies should be considered high-risk and monitored closely both by the nephrologist and obstetrician, and the patient should be counseled appropriately.

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