COMMENTARY

Renal transplant recipients who become pregnant: New insights from histopathology

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INTRODUCTION

Due to enhanced fertility, a greater quality of life, and a reduced likelihood of pregnancy complications compared to those receiving dialysis, it is frequently advised to women with advanced CKD to wait to get pregnant until after a kidney transplant. Despite this, preeclampsia affects 25% to 30% of women who become pregnant after a kidney donation, and preterm birth occurs at a mean gestational age of 35 weeks to 36 weeks. Pregnancy after a kidney transplant is still associated with a significant risk of unfavourable consequences.

The effects of pregnancy on graft loss are of major concern to both women with advanced CKD anticipating transplant and those with working kidney transplants pursuing preconception counselling, in addition to the impact of a kidney transplant on maternal and foetal outcomes. S3 found a higher rate of death-censored graft loss when pregnancy occurred within 1 years to 2 years following transplant, the timing of conception may be important. Some women with advanced CKD may decide to carry a pregnancy with their native kidneys if it is linked to long-term graft loss, knowing that dialysis may be utilised as a stopgap measure before a postpartum transplant (albeit this is most easily achieved with a living donor on standby). Knowing that they could lose a kidney graft during pregnancy can influence a woman's decision to become pregnant or to consider other options, such adoption or a gestational carrier.

We sought to determine if pregnancy led to graft loss over time in this multicenter retrospective analysis. In a novel approach, the scientists examined the effect of pregnancy on allograft histology using protocol and advised allograft biopsies carried out up to 10 years after the transplant. The authors were able to study >36,000 serum creatinine values from 816 women of reproductive age at the time of transplant in order to assess glomerular filtration rate (GFR) deterioration. They discovered that after pregnancy, women who had been pregnant had a statistically significant increase in the estimated GFR decline rate per year of 2.4 ml/min per 1.73 m2 compared to 1.9 ml/min per 1.73 m2 in those who had not been pregnant (P 0.001). To compare the rate of deterioration in these 2 groups, it is unclear whether the time after transplantation is taken into consideration, although it should be emphasised that pregnancies happened at a median of 59.5 months after transplant. The authors, on the other hand, did not discover a difference in graft loss or a loss of >50% of GFR over a median of 8 years of follow-up time, even with an accelerated drop in estimated GFR over time. This is concerning, because it is obvious that a longer period of observation may be necessary to completely understand how pregnancy affects the allograft. However, a subsequent meta-analysis discovered comparable findings, including a slightly elevated blood creatinine level within 2 years postpartum (0.18 mg/dl, 95% CI 0.05-0.32, P = 0.01) without risk for long-term graft loss from >10 years of follow-up data. 5 Preconception hypertension, a creatinine level greater than 1.5 mg/dl, and proteinuria have all been linked in the past to graft loss risk factors.

Surprisingly, in this group, pre-existing hypertension and GFR 60 ml/min were not significant risk factors for loss of GFR, albeit disease severity is poorly documented and GFR may have been clustered around roughly 60 ml/min. Only three women had preconception proteinuria levels that were considered to be considerable (>300 mg/dl), which limits the inferences that can be made about this group, although it did appear to be a factor in the significantly faster postpartum loss in kidney function.

The scientists examined 37 women who had pregnancies that lasted longer than 20 weeks, and they discovered that 21 postpartum biopsies and 33 prepartum biopsies had considerably higher scores

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for vascular fibrous intimal thickening. The period since the transplant or the existence of hypertension at the time of conception could not explain this. The authors reported that 37% of pregnancies were complicated by preeclampsia, although it is unclear whether there was a greater degree of vascular fibrous intimal thickening following a preeclamptic pregnancy because of the limited sample size. For our patients' comfort, the postpartum biopsies' changes were generally similar with the traits seen in allografts over time, such as increasing arteriolar hyalinosis, worldwide glomeruli sclerosis, and interstitial fibrosis/tubular atrophy. Additionally, there was no increased risk of recurrence in the allograft following pregnancy, despite the fact that glomerulonephritis was the most typical cause of end-stage kidney disease prior to transplant.

It is unclear what might be causing kidney transplant recipients' graft loss or decreased GFR during pregnancy. It is well recognised that preeclampsia can lead to glomerular endotheliosis, which typically resolves after delivery. However, population-based studies have shown that preeclampsia is linked to a higher risk of CKD and end-stage kidney disease, and that the development of chronic hypertension following preeclampsia may be caused by a modest endothelial damage. Additionally, compared to controls, biopsies connected to pregnancy are more likely to show focal segmental glomerular sclerosis.

It is crucial to assess this outcome within a larger cohort, in particular across women with and without preeclampsia, given the greater postpartum vascular abnormalities. It is important to assess how aspirin use to prevent preeclampsia affects kidney transplant recipients and whether treatment (and/or a dose response) might be able to counteract these results. It may also be advantageous to maintain blood pressure (BP) during pregnancy more aggressively. We know from the CHIPS trial that aiming for a lower diastolic BP of 85 mm Hg did not increase risk of pregnancy loss and decreased frequency of severe maternal hypertension, even though BP targets in pregnancy for women with CKD normally target a BP level 140/90 mm Hg. Overall renal histopathology offers convincing insight into one possible mechanism behind pregnancy-induced GFR reduction. Unfortunately, judgments on vitally essential yet uncommon clinical outcomes, such as allograft failure and allograft rejection, cannot be reached because to the limited sample size. The effects of pregnancy-related hypertension and the emergence of preeclampsia on the histology of allografts are also unknown. There is currently no indication that pregnancy itself significantly accelerates graft loss over time, therefore we should reassure our patients that this is not the case until larger and longer-term studies are completed.

The likelihood for a slight, although statistically significant, GFR reduction after childbirth and possibly persistent vascular alterations in the allograft are added by Kattah et al. to our preconception advice. The risk of preeclampsia and preterm birth is still very high in pregnancies that are pursued after a kidney transplant for women with advanced CKD or a working kidney allograft. The best maternity treatment is provided in a multidisciplinary clinic that offers both maternal-fetal medicine and nephrology. To assist lower the risk of preeclampsia, low-dose aspirin should be added to their arsenal ofmedications and should be started after 12 weeks of pregnancy. In order to diminish negative effects for the mother and foetus as well as perhaps slowing postpartum GFR decline, it is also prudent to optimise blood pressure and proteinuria before becoming pregnant while maintaining stable graft function.

For many women with CKD, being a mother is a lifelong dream, and taking care of our patients at this time is rewarding and fulfilling. Transparency about the knowns and unknowns of obstetric nephrology fosters better bonds with our patients as they travel this frequently trying and challenging path. We commend Kattah et al. for their use of histopathology to open the door for bigger investigations assessing mechanisms of pregnancy-associated progression of CKD, even if concerns still surround the cause and relevance of both postpartum GFR decrease and vascular alterations in the allograft.