

## ***Long-term evaluation of treatment outcomes in pregnant patients after kidney transplantation***

### **Abstract**

#### **Introduction**

Chronic kidney disease (CKD) and its terminal stage – end-stage renal disease (ESRD) represent a major global health challenge, both for public health and clinical care. With a growing number of patients requiring renal replacement therapy, kidney transplantation (KTx) has become the recognized and preferred treatment for ESRD. Owing to substantial improvements in survival, quality of life, and cost-effectiveness, KTx today is the gold standard compared with long-term dialysis. Advances in transplant surgery, immunosuppression, and postoperative care have enabled successful transplantation from both living and deceased donors. Nevertheless, transplantation entails numerous clinical and ethical challenges. Key ongoing issues include limited organ availability, the risk of rejection, infections, immunosuppression-related malignancies, and long-term metabolic complications.

Advances in transplantation and immunosuppressive pharmacotherapy over recent decades have markedly improved survival among recipients of vascularized organ transplants. As quality of life has increased, a growing number of women of reproductive age opt for pregnancy after transplantation. Pregnancy in organ transplant recipients, however, poses specific clinical challenges—both because of the increased risk of obstetric complications and the potential impact on graft function. Evidence from the available research indicates that while pregnancy after transplantation can have a favorable outcome, it is associated with higher risks of gestational hypertension, preeclampsia, preterm birth, and fetal growth restriction. Long-term monitoring of graft function and of maternal and child health is therefore essential. Nevertheless, definitive data on long-term outcomes remain limited, particularly regarding differences by transplant type, immunosuppressive regimen, and the interval between transplantation and conception.

## **Objectives**

The aim of this doctoral thesis was to perform a long-term, comprehensive analysis of treatment outcomes in women who became pregnant after kidney transplantation (KTx). The study sought to evaluate the impact of pregnancy on maternal clinical status, fetal development and graft function, with particular emphasis on:

- comparative analysis of outcomes in transplant recipients versus a control group;
- assessment of the relationship between the interval from transplantation to conception and fetal development;
- evaluation of the effect of immunosuppressive therapy on pregnancy course, fetal survival and subsequent child development;
- assessment of the impact of pregnancy on graft survival and function;
- analysis of preconception preparation and its importance for pregnancy course and outcome.

The study also addressed the hypothesis that pregnancy in organ recipients can affect graft function, and that appropriate medical preparation and multidisciplinary care can substantially improve prognosis for both mother and child.

## **Materials and Methods**

This retrospective study analyzed medical records of pregnant women after kidney transplantation (KTx). The review was conducted between January and June 2022 and included patients of the University Center for Women's and Neonatal Health, Medical University of Warsaw. The dataset of KTx recipients was compiled between March and July 2021 and comprised patients under the care of the Department of Transplantation Medicine, Nephrology and Internal Medicine, Medical University of Warsaw. Written permission to conduct the study was obtained from the heads of the aforementioned departments.

Study material comprised 67 women who became pregnant after kidney transplantation between 2001 and 2018. For comparative analysis, a control group of 114 women was assembled, consisting of:

- 50 pregnant women without prior organ transplantation,
- 64 kidney transplant recipients who were not pregnant.

The analysis was based on medical records, including data on the course of pregnancy, delivery outcomes, maternal and neonatal health, and graft function during the peripartum period and later periods. The study was conducted in accordance with the Declaration of Helsinki and applicable legal regulations. The project received a positive opinion from the Bioethics Committee of the Medical University of Warsaw (approval no.: AKBE/54/2021).

## Results

The study included 67 women who became pregnant after kidney transplantation (median age at delivery 30 years, median time from transplantation 6 years). The cohort exhibited a moderate decline in renal function between 2018 and 2021 (median  $\Delta$ eGFR  $-7.4$  mL/min/1.73 m $^2$ ) and a modest increase in serum creatinine. Baseline eGFR in 2018 was a significant predictor of eGFR in 2021 ( $\beta = 0.69$ ,  $p < 0.001$ ) and was associated with a lower risk of graft loss. The graft loss rate at 10 years was 9.3%. Higher creatinine levels (pre-pregnancy, during pregnancy and post-partum) were strongly correlated with an increased risk of graft loss (e.g., pre-pregnancy HR = 7.64,  $p < 0.001$ ). Compared with the control group, kidney transplant recipients delivered earlier (median 36 vs. 39 weeks), had infants of lower birthweight (median 2520 g vs. 3410 g), and showed substantially higher rates of fetal growth restriction and preterm birth. In logistic models, transplant status was a strong predictor of fetal growth restriction (OR 26.7) and preterm delivery (OR 66), whereas BMI and pregnancy-induced hypertension were not significant predictors in these models. Better baseline graft function was associated with more favorable graft prognosis, but pregnancy in transplant recipients was linked to a higher risk of adverse perinatal outcomes.

## Conclusions

Pregnancy after kidney transplantation is feasible and can result in favorable outcomes for both mother and child, but it is associated with an increased risk of obstetric complications, including gestational hypertension, preeclampsia, preterm delivery and intrauterine growth restriction (IUGR). Graft function does not deteriorate significantly during a well-managed pregnancy, provided that medical recommendations are followed, the patient is adequately prepared, and care is provided by a multidisciplinary team. The interval between transplantation and conception is an important determinant of pregnancy and fetal outcomes - the best results are observed in women who conceive at least 1-2 years after transplantation. Immunosuppressive therapy during pregnancy should be based on regimens considered

relatively safe (calcineurin inhibitors, azathioprine, low-dose glucocorticoids), whereas agents with proven teratogenic risk (notably mycophenolate) are contraindicated and should be substituted prior to planned conception.

Pregnancy in organ recipients does not adversely affect long-term graft survival provided graft function is stable before conception and immunosuppressive therapy is individually optimized. Adequate preconception preparation - including optimization of immunosuppression, blood pressure control and assessment of graft function - substantially improves peripartum prognosis and reduces the risk of complications.

The findings of this thesis underscore the need for close monitoring of transplant recipients who plan pregnancy and for their management in centers with established experience in the care of pregnant transplant patients.