

# Pregnancy After Renal Transplantation: Ten-Year Single-Center Experience

A. Ghafari and H. Sanadgol

## **ABSTRACT**

There has been an increase in the number of pregnancies among renal transplant recipients. Our experience included 61 pregnancies in 53 patients from January 1997 to April 2007, with 6 patients having multiple pregnancies. Patients were studied for clinical, obstetrical, and perinatal outcomes. The mean patient age was 24.5 years (range, 19–38). They all received living donor kidneys. The mean transplantation-pregnancy interval was 2.7 years (range, 1.7-5.3 years). Immunosuppressive drugs consisted of cyclosporine (CsA), mycophenolate mofetil (MMF), and prednisolone (pred) in 38 patients (72%); CsA, azathioprine (AZA), plus pred were used in 15 patients (28%). Pregnancy complications were chronic hypertension in 21 patients (40%), anemia in 28 (52.6%), and urinary tract infection in 18 (34%). Twelve patients (22.6%) received blood transfusions. Pre-eclampsia was diagnosed in 14 cases (26.4%) and renal dysfunction in 11 (20.7%) with pre-eclampsia assumed to be the main cause. Three patients (5.6%) had graft losses as a result of hemorrhagic shock, sepsis, and eclampsia. Premature rupture of membranes occurred in 6 cases (11.3%), and preterm delivery occurred in 14 cases (26.4%). Eleven (20.7%) newborns were small for gestational age. One club foot and one large facial hemangioma occurred in 2 infants, respectively. One case of neonatal death was registered as a result of excessive prematurity. One mother died due to sepsis. Cesarean section was performed in 24 patients (45.2%), the main indications being related to hypertension and fetal distress. There were no significant differences between MMF-treated and AZA-treated patients with respect to clinical, obstetrical, and perinatal outcomes. This group of patients was characterized by a wide range of antenatal and perinatal problems that must be managed in specialized tertiary units to achieve the best results. MMF may be as safe as AZA in pregnancy.

WITHIN 6 months after renal transplantation ovulation returns to normal.¹ Indeed, renal function and endocrine status rapidly improve after renal transplantation, and 1 of 50 women of childbearing age become pregnant with a success rate exceeding 90% after the first trimester.² Prenatal management must address potential fetal complications (preterm delivery, intrauterine growth retardation, and low birth weight) as well as maternal complications (hypertension, preeclampsia, gestational diabetes, acute rejection, and graft loss).³ Various studies in renal allograft recipients have been published with successful outcomes of pregnancy.³-5 We hereby have reported the outcomes of pregnancy in our transplant population.

## PATIENTS AND METHODS

From January 1991 to April 2007, we performed 845 renal transplantations in female patients. Excluding unmarried, divorced

From the Nephrology Department, Urmia University of Medical Sciences, Emam Hospital; Urmia, and the Nephrology Department, Zahedan University of Medical Sciences, Zahedan, Iran. Address reprint requests to Ali Ghafari, Nephrology Department Emam Hospital, Ershad st. Urmia University of Medical

subjects, and those who had not completed or had died during the first year posttransplantation, 61 pregnancies were recorded in 53

patients with 6 patients having multiple pregnancies. Parameters included mean age, transplantation-pregnancy interval, immuno-

suppressive drugs, pregnancy complications, urinary tract infec-

tions, blood transfusions, pre-eclampsia, renal dysfunction, graft

loss, fetal outcome, and complications needing Cesarean section.

ment, Emam Hospital, Ershad st, Urmia University of Medical Sciences, Post code: 5715943394, Urmia, Iran. E-mail: ghaf\_ali@yahoo.com

© 2008 by Elsevier Inc. All rights reserved. 360 Park Avenue South, New York, NY 10010-1710 0041-1345/08/\$-see front matter doi:10.1016/j.transproceed.2007.11.052

252 GHAFARI AND SANADGOL

#### **RESULTS**

This study of 61 pregnancies among 53 patients between January 1997 and April 2007 included 6 patients with multiple pregnancies. Mean patient age was 24.5 years (range, 19-38 years) with all having received a living donor kidney. Median duration of conception after transplantation was 31 months (range, 8-86 months). The mean transplantation-pregnancy interval was 2.7 years (range, 1.7–5.3 years). Immunosuppressive drugs consisted of cyclosporine (CsA), mycophenolate mofetil (MMF), and prednisolone (pred) in 38 patients (72%); CsA, azathioprime (AZA), plus pred were used in 15 patients (28%). Pregnancy complications were chronic hypertension in 21 patients (40%). It had progressed in 7 and was new-onset hypertension in 6. Antihypertensives were changed from calcium channel blockers and angiotensin converting enzyme inhibitors to methyldopa. Anemia was noted in 28 patients (52.6%); urinary tract infections were noted in 18 patients (34%). Twelve patients (22.6%) received blood transfusions; albuminuria of trace to 3+ was noticed in 16 of 61 pregnancies. Pre-eclampsia was diagnosed in 14 cases (26.4%) and renal dysfunction in 11 (20.7%) with preeclampsia assumed to be the main cause. Three patients (5.6%) had graft loss as a result of hemorrhagic shock, sepsis, and eclampsia. Premature rupture of membranes occurred in 6 cases (11.3%), and preterm delivery occurred in 14 cases (26.4%). The mean Appar score of the live babies was 7.9 + / - 0.7. Forty-four (61.1%) babies were admitted to the neonatal intensive care unit and early neonatal death occurred in 4 (5.5%). Eleven (20.7%) newborns were small for gestational age. One club foot and one large facial hemangioma occurred in 2 infants, respectively. One case of neonatal death was the result of excessive prematurity. One mother died due to sepsis. Cesarean section was performed in 24 patients (45.2%), the main indications being hypertension syndromes and fetal distress. There were no significant differences between MMFtreated and AZA-treated patients with respect to clinical, obstetrical, perinatal outcomes. At an average follow-up of 32 months (range, 1–10 years) after childbirth, these women maintained their serum creatinine values between 0.8 and 1.8 mg/dL.

## DISCUSSION

Pregnancy, as reported earlier, does not affect long-term graft survival,<sup>2–5</sup> but graft dysfunction and high baseline serum

creatinine at time of conception as well as be associated with poor pregnancy outcomes both. Women who display serum creatinine values of at least 1.75 mg/dL reportedly show further deterioration of graft function in relation to pregnancy.<sup>6,8</sup> This study described satisfactory graft function when females who conceived were followed for as long as 10 years after transplantation. Antenatal and perinatal problems were more frequent in our patients as shown by others<sup>5</sup>: prematurity, intrauterine growth retardation (IUGR), and low birth weight.

There were no significant differences between MMFtreated and AZA-treated patients with respect to clinical, obstetrical, and perinatal outcomes.

In conclusion, conception after transplantation is safe when proper guidelines are followed. Newborns are universally at greater risk of low birth weight. There is concern based on animal reproductive studies that the risks of birth defects and/or spontaneous miscarriages are increased among women exposed to MMF during pregnancy. Of the 9 pregnancies reported to the registry to date, there have been no birth defects among 5 liveborn of female recipients exposed to MMF. Data remain limited. Based on our data MMF may be as safe as AZA in pregnancy, but further studies and probably a meta-analysis are necessary. This group of patients was characterized by a wide range of antenatal and perinatal problems and must be managed in specialized tertiary units to achieve the best results.

### **REFERENCES**

- 1. Ha J, Kim SJ, Kim ST: Pregnancy following renal transplantation. Transplant Proc 26:2117, 1994
- 2. Davison JM: Dialysis, transplantation and pregnancy. Am J Kidney Dis 17:127, 1991
- 3. del Mar Colon M, Hibbard JU: Obstetric considerations in the management of pregnancy in kidney transplant recipients. Adv Chronic Kidney Dis 14:168, 2007
- 4. First MR, Coombs CA, Weiskittel P, et al: Lack of effects of pregnancy on renal allograft survival or function. Transplantation 59:472, 1995
- 5. Sturgiss SN, Davison JM: Effects of pregnancy on long-term function of renal allograft: an update. Am J Kid Dis 26:54, 1995
- 6. Santamaria Saber LT, Duarte G, Costa JAC, et al: Pregnancy and renal transplantation: experience in a developing country. Am J Kid Dis 3:465, 1995
- 7. Thompson BC, Kingdon EJ, Tuck SM, et al: Pregnancy in renal transplant recipients: the Royal Free Hospital experience. Q J Med 96:837, 2003
- 8. Armenti VT, Rsdomski JS, Mortiz MJ, et al: Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. Clin Transpl 97:11, 2002