Pregnancy and Delivery in the Sequel of Kidney Transplantation: Single-Center Study of 8 Years' Experience

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ABSTRACT

Background. Depending on hyphothalamic, hyphophyseal, and gonadal axis dysfunction, anovulatory irregular cycles occur and the probability of pregnancy decreases in the patients with chronic kidney disease (CKD). Maternal mortality and morbidity rates are increased in CKD patients; the risk of premature delivery is 70% and the risk of preeclampsia is 40% more than normal among those with a creatine level of >2.5 mg/dL.

Methods. If a pregnancy is expected in the sequel of kidney transplantation (KT), a multidisciplinary team approach should be adopted and both the gynecologist and the nephrologist should follow the patient simultaneously. Among 3883 patients who underwent KT at Antalya Medical Park Hospital Transplantion Department between November 2009 and October 2016, the records of 550 female patients between the ages of 18 and 40 years were examined retrospectively; 31 patients who complied with these criteria were included in the study group. In 6 of these patients who had an unplanned pregnancy, medical abortion was performed after the families were informed about the possible fetal anomalies caused by the use of everolimus in the first trimester, and they were excluded from the study (pregnant group). The control group consisted of 43 patients who had a KT and became pregnant, and of those who had recently undergone KT and shared similarities regarding age, CKD etiology, duration of dialysis, and number of transplants.

Results. In both groups, the ages of the patients, their follow-up span and dialysis duration, tissue compatibility, age of the donor, and time elapsed until the pregnancy was analyzed, whereas in the control group, creatinine levels in the first, second, third, and fourth years after the KT were reviewed. Additionally, in the pregnant group, creatinine levels of the first, second, and third trimesters; delivery week; birth weight of the baby; APGAR scores of the first minute; postnatal creatinine levels of first, second, and third years; and prenatal, maternal, and postnatal acute rejections were reviewed. We measured the creatine clearance by use of the Cockcroft-Gault formula in the pregnancy group before pregnancy and during delivery [Cockcroft-Gault formula: $(140 - \text{age}) \times \text{body weight (kg)}/72 \times \text{plasma creatine level (mg/dL)} \times 0.85$].

Conclusions. Pregnancy after KT is risky both for the mother and the baby; however, if planned and followed in coordination within an experienced center, both the pregnancy period and the birth process can occur without distress.

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THE FIRST case of pregnancy after a kidney transplant (KT) was reported in 1956 in a patient who underwent a KT from her twin sister, and it was a breakthrough regarding pregnancy in the sequel of a KT [1]. Nearly 14,000 pregnancy cases have been reported within the literature [1].

Depending on hypothalamic, hyphophyseal, and gonadal axis dysfunction, anovulatory irregular cycles occur and the probability of pregnancy decreases in patients with chronic kidney disease (CKD) [2–4]. Maternal mortality and morbidity rates are increased in CKD patients; the risk of premature delivery is 70% and the risk of preeclampsia is 40% more than normal among those with a creatine level >2.5 mg/dL [2].

After KT, menstrual ovulatory cycles and sexual dyfunctions return to normal in the following 12th month, and generative fertilization begins [4,5]. There is no certain aggreement on the scheduling of pregnancy. Whereas the American guidelines suggest waiting for at least 1 year after KT, the European guidelines advise waiting for 2 years [4]. The American Society of Transplantation advises that pregnancy should be postponed for at least 1 year, graft functions should be normal (with a creatine level <1.5 mg/dL), proteinuria should be minimal, and there should be no infections that could affect the fetus (such as cytomegalovirus) or hypertension. Depending on pregnancy after KT, both maternal and fetal risks exist such as rejection, loss of graft, preecylampsia, diabetes, preterm delivery (<36 weeks) abortus, babies with a low birth weight (<2500 g), and the anomalies of intrauterine growth retardation [4,6]. If a pregnancy is expected in the sequel of KT, a multidisciplinary team approach should be adopted and both the gynecologist and the nephrologist should follow the patient simultaneously [4].

Within this study, the patients who underwent a KT at the Antalya Medical Park Hospital Transplantion Department and became pregnant afterward were examined retrospectively; the rate of pregnancy after KT, comparisons of similar controls of the pregnant group, and the graft functions of the patients who gave birth after KT compared with those who did not deliver a baby were analyzed.

METHODS

Among 3883 patients who underwent KT at Antalya Medical Park Hospital Transplantion Department between November 2009 and October 2016, the records of 550 female patients between the ages of 18 and 40 years were examined retrospectively. The criteria to be included in this study were determined as being pregnant after KT and giving birth. Thirty-one patients who complied with these criteria were included in the study group. In 6 of these patients who had an unplanned pregnancy, medical abortion was performed after the families were informed about the possible fetal anomalies caused by the use of everolimus in the first trimester, and they were excluded from the study (pregnant group). The control group consisted of 43 patients who had a KT and did not become pregnant. The control group has similarities regarding age, CKD etiology, duration of dialysis, and number of transplants. In both groups, the ages of the patients, their follow-up span and dialysis duration, tissue compatibility, age of the donor, the time elapsed until the pregnancy were analyzed, whereas in the control group, creatinine levels in the first, second, third, and fourth years after the KT were reviewed. Additionally, in the pregnant group, creatinine levels of the first, second, and third trimesters; delivery week; birth weight of the baby; APGAR scores of the first minute; postnatal creatinine levels of first, second, and third years; and prenatal, maternal, and postnatal acute rejections were measured. We measured the creatine clearance by use of the Cockcroft-Gault formula in the pregnancy group before pregnancy and during delivery [Cockcroft-Gault formula: (140 − age) × body weight (kg)/72 × plasma creatine level (mg/dL) × 0.85].

During the prenatal follow-up of the patients, a scanning test between the 11th and 14th weeks in the first trimester, a fetal anomaly scanning between the 20th to 22nd weeks, and gestational diabetes scanning with 50 g oral glucose between the 24th and 28th weeks were applied.

All patients in the pregnant group and the control group had a KT from a live donor. As immune-suppressive agents, calcineurin inhibitors (CNI) (tacrolimus and cyclosporine) and oral steroids were used. For those patients who deliberated to have a planned pregnancy, micophenolate mofetil and m-TOR inhibitor medications were discontinued in the preceding 3 months. Calcineurin inhibitor doses increased after pregnancy occurred, but there was no change in steroid dose. After pregnancy occurred, routine follow-up of pregnant patients increased to monthly until 24 weeks of gestation, then twice a month until the 32nd week, and then weekly until delivery.

Regarding statistical analysis, the SPSS16 version was used; the average, standard deviation, and median parameters were viewed, and a value of $P < .05$ was regarded as statistically significant.

RESULTS

In the pregnant group, 25 patients were examined and average indications were studied as follows: age, 27.2 ± 4.0 years (22–36); follow-up span, 77.1 ± 16.4 months (31.9–96.1); dialysis duration, 20.2 ± 36.1 months (0–145); and tissue compatibility, 3.2 ± 1.5 (1–6).

In the control group, 43 spatients were examined; average values were as follows: age, 25.6 ± 3.9 years (22–36); follow-up span, 74.1 ± 14.2 months (48–92); dialysis duration, 20.7 ± 11.4 months (0–145); tissue compatibility, 3.2 ± 1.5 (1–6); and age of the donor, 42.6 ± 11.4 years (24–57).

In the pregnant group, 22 patients had KT once and 3 patients had it twice, whereas in the control group, 38 patients had KT for the first time and 5 patients had it for the second time. In the pregnant group, 10 patients were preemptive, 27 patients were undergoing hemodialysis, and 3 patients were receiving peritoneal dialysis.

In the pregnant group, postnatal creatinine levels were as follows: in the first year, 1.0 mg/dL (0.5–1.6); the second year, 1.0 mg/dL (0.6–1.3); the third year, 0.9 mg/dL (0.5–1.3); and the fourth year, 1.0 mg/dL (0.6–1.3). In the control group, creatine levels after KT were 0.9 mg/dL (0.4–2.1) in the first year, 0.9 mg/dL (0.5–2.0) in the second year, 0.9 mg/dL (0.5–1.8) in the third year, and 1.1 mg/dL (0.4–4.8) in the fourth year.