

## PREGNANCY IN RENAL TRANSPLANT RECIPIENTS

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### ABSTRACT

**Background:** Correction of the uremic state by a functioning allograft often restores fertility in women of reproductive age. The rate of fertility significantly differs between industrial countries, developing and middle east countries. On the other hand the results of pregnancy in Kidney Transplantation (KTP) patients are significantly better than hemodialysis patients, and pregnancy most often has no side effects on the function of the transplanted kidney.

**Objectives:** The purpose of this study is to investigate the rate of fertility and results of pregnancy among KTP women, and the assessment of the function of transplanted kidneys during pregnancy among those who have received kidneys in Golestan Hospital from 1996 to 2003.

**Methods:** All the transplanted women in child bearing age who were interested in accepting pregnancy were involved in this study. After pregnancy, all the patients were visited twice a month until the 32nd week of pregnancy and their histories were taken and regular clinical examination and necessary paraclinical assessments were carried out. After the 32nd week, they were visited weekly and other necessary assessments were done in addition to previous measures. Taking immunosuppressive drugs was continued with a minor dose reduction and consumption of harmful drugs like some antihypertensives was prohibited.

**Results:** 16 out of 48 women who were at child bearing age and were interested in pregnancy got pregnant and totally 22 cases of pregnancy occurred. Four cases resulted in spontaneous or therapeutic abortion and 3 out of 18 remaining cases had intrauterine fetal death and the others had successful pregnancy. The most common complication was LBW and following that premature labor. Maternal complications were no more than the general population and the function of the transplanted kidney had no decline in most of the cases.

**Conclusion:** Based on what was mentioned, it is concluded that successful KTP can increase the chance of pregnancy and in order to improve the results of pregnancy, it is necessary to prepare ideal conditions especially for the transplanted kidney before pregnancy, while pregnancy does not produce any decline in the function of the transplanted kidney.

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**Keywords:** Pregnancy, Premature labor, Kidney transplantation, Low birth weight (LBW).

### INTRODUCTION

Uremic state correction through kidney transplantation with normal function may frequently restore fertility in

women of child bearing age.<sup>1, 2</sup> In western countries, it seems that 2 to 3% of women at child bearing age get pregnant after kidney transplantation.<sup>1, 2</sup> The average fertility rate in developing countries is more than developed ones.<sup>4</sup> In Brazil 14% of women in child bearing age got pregnant after transplantation.<sup>5</sup> In Oman a fertility rate of 31% and in Saudi Arabia 50% were reported.<sup>6, 7</sup>

On the other hand, pregnancy results in transplant recipients are obviously better than results among dialysis

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patients. In a wide assessment, successful pregnancies of about 92% were reported omitting therapeutic and spontaneous abortions.<sup>8</sup> An incidence of spontaneous abortion of 13% was reported which showed no difference with the general population but one third of pregnant transplanted patients desire to do therapeutic abortion that is probably due to incomplete family control programming in women whom did not think they could get pregnant.<sup>9</sup>

The most important fetal complication is premature delivery which occurs in 45 to 67% of patients, while this rate is about 5% in the general population<sup>5</sup>. This complication may be due to different causes such as urinary infection, premature rupture of membranes, obstetric intervention due to uncontrolled hypertension and fetal distress.<sup>5</sup> Low birth weight is one of the other complications which from 20-30% to 64% has been reported.<sup>9, 6</sup> No fetal abnormality has been reported.<sup>9</sup>

Pregnancy results in transplanted women treated by cyclosporine are similar to the others.<sup>10, 11</sup> Blood pressure rises in 67% of pregnant transplanted women<sup>5</sup> and the rate of preeclampsia is reported from rare to 30%<sup>10, 11</sup> and these two are the most important maternal complications. Urinary infection is seen in 86% of pregnant transplanted women.<sup>5</sup> Acute rejection occurred in 9% of cases that is not more than that of nonpregnant women.<sup>7</sup> Pregnancy has no harmful effect on the short term and long term course of kidney transplantation and the rate of kidney loss, chronic rejection and mortality does not increase.<sup>2, 12-14</sup>

The aim of this study is assessment of fertility rate and pregnancy results in transplanted women and study of transplanted kidney function during pregnancy in transplanted women in Ahwaz Golestan hospital from 1996 to 2003.

## PATIENTS AND METHODS

All of the transplanted women at child bearing age who were interested in pregnancy and did not use any contraceptive device were assessed in this study. Before fertilization, measures and assessments were done as follows:

The patients were recommended not to get pregnant at least during the first year after transplantation and preferably more than 2 years for unrelated donors and more than 1 year for related ones. Patients' blood pressure was controlled through diet or proper antihypertensive drugs which did not have any contraindication in pregnancy. Kidney function was assessed by measurement of serum creatinine. Urinalysis for protein and urine culture for urinary infection and kidney sonography were also done. On the condition that the patient's creatinine was less than 2 mg/dL and preferably less than 1.5 mg/dL, urinalysis protein was 0 or maximally 1+, no sign of urinary infection and normal kidney sonography, and no urologic abnormality like hydronephrosis was seen, the patient was allowed to get pregnant. In the case of urinary infection, pregnancy was delayed until complete treatment of infection by proper antibiotics.

After pregnancy, patients were visited twice a month until the 32<sup>nd</sup> week of pregnancy and after that weekly until term and during each visit in addition to taking proper history, physical examination with emphasis on blood pressure, weight, edema, size of uterus and fetal heart ultrasound was done. During the first visit and later, necessary tests including: CBC, FBS, TG, cholesterol, urea and creatinine, Na<sup>+</sup> and K<sup>+</sup>, liver enzyme and bilirubin, uric acid, U/A and U/C were done monthly. In the first visit HBsAg, VDRL and GTT with 50 g of glucose were done. For assessing the safety of the fetus and placenta and volume of amniotic fluid, sonography was done at the 8<sup>th</sup> week and once during the 20<sup>th</sup> to 24<sup>th</sup> week and later if necessary. Kidney sonography in mid and late pregnancy was repeated. Fetus safety tests including NST (non-stress test) and biophysical profile were done from the 32<sup>nd</sup> week of pregnancy. Patients were treated by taking folic acid 1mg daily and ferrous sulfate tablets 150 mg and multi-vitamins if necessary.

All of the patients were treated by triple immunosuppressive protocol including prednisolone 10 mg daily, cyclosporine 3-4 mg/kg and azathioprine 1.5 mg/kg. Antihypertensive drugs were changed if necessary and ACE inhibitors were specifically prohibited. In case of loss of any maternal or fetal indication in premature labor, the patients were permitted to continue pregnancy up to term. The dose of steroids was increased during delivery to reduce labor stress and its effect on kidney rejection after pregnancy termination. In case of loss of obstetrical indication vaginal delivery and in other cases C/S was permitted. Statistical analysis was performed by SPSS software, using paired t and chi-square tests. A *p* value of less than 0.05 was regarded as significant.

## RESULTS

Among 130 transplanted female patients, during 1996–2003, 80 were in reproductive age. 48 of them had tendency for conception. Average age of them was 28 years old (range of 17-38). Of the 48 patients, 16 had been pregnant (22 pregnancies totally) (33%). Of the 22 pregnancies 2 terminated by spontaneous abortion and 2 terminated by therapeutic abortion (one due to psychologic problems and the other due to severe impairment of the transplanted kidney). Of 18 other pregnancies which continued, 6 terminated by preterm delivery (before 37 weeks of GA), 3 due to premature rupture of membranes, recurrent urinary infection and preeclampsia, and 3 due to unknown causes.

Of the continued pregnancies, 3 terminated by IUFD, two of these 3 IUFDs occurred in one patient. This patient had a creatinine of 2.2 in the initiation of the first pregnancy and a creatinine of 2.5 in the second pregnancy. In this patient, IUFD occurred in 24 and 26 weeks of pregnancies due to fetal growth restriction.

Of the continuing pregnancies, 9 had full-term delivery. Of the healthy born infants, 10 were low birth weight (less than 2.5 kg). No congenital anomaly was demonstrated. Urinary infection occurred in 30% of patients, which was controlled by antibiotic therapy.

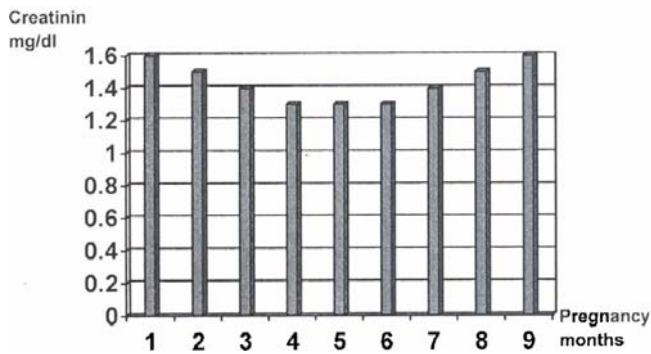


Fig 1. Change of mean serum creatinine in pregnant patients.

Suppression therapy was administered due to recurrent infection in 2 of them.

Pre-eclampsia occurred in 2 patients, and pre-term delivery occurred in one of them, in spite of conservative treatments.

Hypertension developed in half of the patients and was controlled by antihypertensive drugs. No ectopic pregnancy was demonstrated. Impaired renal function developed in one patient, which led us to perform therapeutic abortion. Clinical and paraclinical evidence demonstrated an acute kidney rejection (the patient did not agree with kidney biopsy). After therapeutic abortion, pulse of methylprednisolone was administered and renal function became normal. At the beginning and at the end of pregnancy, average serum creatinine had no change ( $p > 0.05$ ) (Fig. 1).

All patients underwent normal vaginal delivery except 2 cases who underwent cesarean section due to obstetrical indications.

## DISCUSSION

Considering the 0.5% incidence of pregnancy in dialysis patients (per year) and the poor outcome of pregnancies<sup>15</sup>, the incidence and outcome of pregnancies have improved following transplantation.<sup>9</sup> Following kidney transplantation, the incidence of pregnancy in industrialized countries is 2-3%, but is 33% in our study which is comparable to other third world and middle-east countries.<sup>4-6</sup>

The incidence of spontaneous abortion in transplanted patients is the same as in the general population and other studies, but the incidence of therapeutic abortion is significantly lower than other studies. It is probably due to differences in indication and legal rules of therapeutic abortion in our country.

The most common fetal complication was low birth weight (55%), which is significantly higher than other studies. This is probably due to cyclosporine. Several studies revealed that cyclosporine consumption has no influence on fetal complications but can cause low birth weight.<sup>16</sup>

Preterm delivery was 33% in our study although it is the most common fetal problem in other studies.<sup>5</sup> Success rate of pregnancies was 83% which is comparable to other studies.<sup>9,10</sup>

The incidence of hypertension, toxemia of pregnancy and urinary infection is comparable to other studies.<sup>5</sup>

The rate of acute kidney rejection was 9%, comparable to other reports and the general population.<sup>7</sup> Pregnancy did not impair renal function, and serum creatinine showed no change during pregnancy ( $p > 0.05$ ). Although pelvic osteodystrophy increases in these patients due to renal failure, previous dialysis and/or steroid administration<sup>16</sup>, only 11% of our patients needed cesarean section for delivery, which is less than the general population. This is probably due to low birth weight of infants which facilitates normal vaginal delivery.

## CONCLUSION

Successful kidney transplantation can increase fertility rates comparing to dialysis, without any renal function impairment during pregnancy.

For lowering pregnancy complications, we have some suggestions:

- The minimum time from transplantation should be one year.
- Serum creatinine (should) be less than 2 mg/dL (preferably 1.5).
- No acute kidney rejection in recent months.
- Good control of blood pressure.
- Proteinuria in normal range or slightly more than normal.
- Normal sonographic of urologic appearance of the transplanted kidney.
- Decrease dose of immunosuppressive drugs.
- Avoidance of harmful drugs.

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