

# Outcome of Pregnancy Following Renal Transplantation

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## Summary

Successful renal transplantation improves fertility with 1 in 50 women of childbearing age becoming pregnant. Pregnancy following renal transplantation is associated with increased maternal and fetal complications. In Belfast 118 women of childbearing age (15-45 yrs) have received a renal allograft and of these 14 (12%) have become pregnant. Twenty-seven pregnancies have resulted in 23 live births (including one set of identical twins), 1 still birth and 4 first trimester abortions. The most frequent complications were hypertension and prematurity. In this group of patients, whose sole immunosuppressive therapy was azathioprine and prednisolone, pregnancy post transplantation was associated with frequent successful outcome and a low incidence of maternal and fetal complications.

## Introduction

Renal transplantation is the preferred form of renal replacement therapy in women of childbearing age. Sexual dysfunction is common in female patients having dialysis therapy and only about 1 in 200 women of childbearing age conceive whilst receiving this form of renal replacement therapy<sup>1</sup>. Few of these pregnancies in female dialysis patients result in live births at term<sup>1-4</sup>. Successful renal transplantation is associated with improved rehabilitation and in many women an increase in fertility. The conception rate following renal transplantation is reported to be increased to 1 in every 50 women of childbearing age<sup>5</sup>. Pregnancy following renal transplantation is associated with a number of fetal and maternal risks<sup>6</sup>. Maternal complications include worsening renal function<sup>7,8</sup> and hypertension<sup>9-10</sup>. Fetal problems include prematurity, growth retardation and congenital infections<sup>8-12</sup>.

This paper describes the outcome of pregnancy following renal transplantation in a single centre over a 25 year period where azathioprine and prednisolone have been the sole immunosuppressive agents prescribed for women of childbearing age.

## Patients and methods

The Regional Nephrology Unit, located at the Belfast City Hospital, Northern Ireland, serves a population of 1.5 million. During the period 1965 to 1989 a total of 118 women of childbearing age (15-45 yr) have received a cadaveric renal allograft at this centre. All patients were treated with azathioprine (3 mg/kg) and low dose oral prednisolone as previously reported<sup>13</sup>. A total of 27 pregnancies have been confirmed in 14 (12%) women following transplantation. The women have been followed-up post transplantation for a mean of 10.9 years (range 3-17 yr). The aetiology of the end stage renal disease in these women is shown in Table I. The details of these pregnancies, together with the fetal and maternal outcomes, have been reviewed.

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## Results

The mean age at transplantation was 23 yr (range 18-31 yr) and the mean age at first conception following transplantation was 27 yr (range 23-34). The interval between transplantation and first conception ranged from 1 to 11 years (mean 49 months). A total of 23 live births (including one set of identical twins) have resulted from the 27 confirmed pregnancies in these 14 women. Of the remaining pregnancies 4 were lost as spontaneous first trimester abortions and the other resulted in a stillbirth after 8 months gestation.

**Maternal Complications:** Graft function at the time of conception was excellent (mean serum creatinine 103±24 umol/l). Only one of the pregnancies was associated with a documented decline in graft function (serum creatinine rising from 100 umol/l at conception to 144 umol/l at term) and this deterioration resolved following delivery. Three patients were hypertensive prior to conception and all were taking anti-hypertensive drugs. Hypertension developed during pregnancy in a further 4 patients necessitating their admission to hospital and two of these patients were treated with anti-hypertensive drugs. No pregnancies were complicated by acute rejection. Caesarean section was performed on 8 (35%) patients for the following reasons: fetal distress (3), previous caesarean section (2), slow progression of labour (1) previous still birth (1) and twins (1). The remaining infants were delivered vaginally. Unfortunately one of the mothers who was hypertensive prior to and during pregnancy died 4 months after pregnancy from a subarachnoid haemorrhage. All other patients with confirmed pregnancies survive with the duration of follow up pregnancy ranging from 1 to 12 years (mean 6.5 yr).

TABLE I  
Aetiology of Original Renal Disease

Chronic glomerulonephritis	6
Chronic pyelonephritis	3
Hypertensive nephrosclerosis	1
Reflux nephropathy	1
Unknown	3
<b>TOTAL</b>	<b>14</b>

**Fetal Complications:** There were 23 live births (including one set of identical twins) with 12 male and 11 female infants delivered. Thirteen infants (including twins) were preterm (born before 37 completed weeks of gestation). Only two infants were considered to be small for gestational age (below the 10th percentile in birthweight for a given gestational age) and both these babies were preterm infants. There were three perinatal deaths including two infants born at 30 weeks who subsequently died from sepsis and one infant born at 25 weeks weighing 650 g who died shortly after birth. The remaining babies have survived without major neonatal complications or congenital abnormalities.

### Discussion

Pregnancy in recipients of renal transplants presents special difficulties both for the patients and the medical and nursing staff caring for them. Pre-pregnancy counselling should include discussion with the patient of the increased risk of maternal and fetal complications in such pregnancies. The higher incidence of premature cardiovascular deaths in renal transplant recipients<sup>14</sup> should be considered whilst counselling prospective parents. However despite these problems over 2000 successful pregnancies have now been achieved in the renal transplant recipients<sup>15</sup>.

In our series the conception rate in women of childbearing age with renal transplants was 12% which is higher than in the report of Lau and Scott<sup>5</sup>. The rate of spontaneous abortion was 15% but this may represent an underestimate as only confirmed pregnancies are included in this report. Preterm labour occurred in 55% of the pregnancies that resulted in a live birth with the majority occurring following premature rupture of the membranes. Previously cited reasons for the higher incidence of premature births in renal transplant recipients include poor maternal renal function, infection of the urinary tract, pregnancy induced hypertension and premature rupture of the membranes<sup>6,7</sup>.

The perinatal mortality was 13% and all the deaths were in premature infants. Sepsis was implicated in at least 2 of the 3 deaths although maternal-fetal transmission of infection could not be established in these cases. No congenital abnormalities were observed in the live births despite the potential risk of teratogenesis associated with the immunosuppressive therapy of azathioprine and prednisolone. Intrauterine growth retardation was not detected clinically during the pregnancies however 13% of these infants were small for gestational age. Intrauterine growth retardation is a frequent complication of pregnancies in renal transplant recipients occurring in 8-45% of cases<sup>5</sup>. There is concern that growth retardation may occur more frequently in patients treated with cyclosporin A<sup>11</sup>.

Hypertension was the major cause of maternal morbidity

occurring in 26% of the pregnancies. Only one of the patients who developed hypertension during pregnancy has developed deterioration in graft function post partum associated with persistent hypertension (creatinine 300  $\mu\text{mol/l}$ ; creatinine clearance 20 ml/min 7 years post pregnancy). Hypertension was a factor in the only maternal death caused by sub-arachnoid haemorrhage.

In common with most other transplant centres our unit now employs cyclosporin A as part of the immunosuppressive schedule post renal transplantation. The outcome of any subsequent pregnancies where cyclosporin A is the main immunosuppressive agent used will be monitored prospectively. In this series of pregnancies in renal transplant recipients azathioprine and prednisolone was associated with a low incidence of maternal and fetal complications and frequent successful outcome of pregnancy.

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