



## Pregnancy Outcome in Women with Primary Renal Disease

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### Abstract

**Background:** The preconception and intraconception parameters that are relevant to outcome in women with underlying renal disease remain controversial.

**Objectives:** To analyze the types and frequencies of short- and long-term (2 years after delivery) maternal and neonatal complications in 38 patients with primary renal disease (46 pregnancies), most of them with mild renal insufficiency.

**Methods:** Logistic regression models were formulated to predict successful outcome.

**Results:** Successful pregnancy outcome (live, healthy infant without severe handicap 2 years after delivery) was observed in 98% of the patients with primary renal disease. Factors found to be significantly predictive of successful outcome were absence of pre-existing hypertension, in addition to low preconception serum uric acid level.

**Conclusions:** Most women with primary renal disease who receive proper prenatal care have a successful pregnancy outcome. Worse pregnancy outcome was observed in women with moderate or severe renal failure. Fitted logistic models may provide useful guidelines for counseling women with preexisting renal disease about their prospects for a successful pregnancy in terms of immediate and long-term maternal and neonatal outcome.

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As recently as 20 years ago, clinicians tended to discourage pregnancy in women with underlying renal parenchymal disease. However, recent studies have suggested that patients with preserved or only mildly decreased renal function and normal blood pressure at conception will fare well [1]. Prognosis is more guarded in the presence of moderately impaired renal function or preconception hypertension; about one-third of such patients will experience renal function deterioration during pregnancy and accelerated progression of the underlying disease after delivery [2,3]. However, except for preexisting hypertension, the correlation of specific preconception and

pregnancy parameters related to the underlying renal disease with maternal and neonatal outcome remains unclear. This makes it very difficult for clinicians to counsel affected women about the advisability of conception or whether to continue a pregnancy already in progress. Counseling should be provided only after thorough evaluation in a tertiary care center by an experienced perinatologist and nephrologist.

The aim of the present study was to calculate the probability of a successful pregnancy outcome in patients with primary renal disease based on pre- and intraconception factors. Pregnancy outcome was assessed on the basis of maternal and infant 2 year follow-up.

### Materials and Methods

Serum creatinine was used as an index of glomerular filtration rate. Renal insufficiency was defined on the basis of serum creatinine concentration as: mild if below 1.4 mg/dl [4], moderate if 1.4–2.4 mg/dl, or severe if 2.5 mg/dl or more. Proteinuria was classified by quantitative measurements as: absent (grade 0) if <20 mg/hour, microalbuminuric (grade 1) if 20–300 mg/24 h (determined by radioimmunoassay technique that was validated for use in pregnancy in our laboratory) [5], low (grade 2) if 300–3,000 mg/24 h, and high (grade 3) if >3,000 mg/24 h. Pre-existing hypertension was diagnosed if diastolic blood pressure exceeded 90 mmHg or if the patient was receiving antihypertensive drugs before pregnancy or before 20 weeks of gestation.

The study population included 38 women (46 pregnancies) with primary renal disease who were admitted to the Hypertension and Diabetes in Pregnancy Clinic of the Rabin Medical Center, Israel between 1990 and 1995. All were followed by local hospital specialists in perinatology, nephrology and endocrinology. Data for the study were collected from the patients' records.

Primary renal disease was classified as either chronic glomerulonephritis or chronic tubulo-interstitial disease on the basis of biopsy findings or the extent of proteinuria and characteristic changes on intravenous pyelography.

Of the 38 cases of primary renal disease, 7 (18%) were diagnosed as IgA nephropathy, 6 (16%) as reflux nephropathy, 5 (13%) as chronic pyelonephritis, 5 (13%) as chronic glomerulonephritis, 2 (5%) as polycystic kidney, and 13 (34%) as other types. Hypertension before and during pregnancy was generally treated with nifedipine.

Patients with imminent preterm delivery were treated with Celestone, and prophylactic antibiotic treatment was added in cases of premature rupture of the membranes.

### Preconception and intraconception parameters

The preconception factors analyzed for the patients were type of primary renal disease, age, parity, evidence of hypertension, grade of proteinuria, and serum creatinine and uric acid levels. Changes in the grade of proteinuria and serum creatinine, creatinine clearance and uric acid levels during pregnancy were also taken into account.

### Short-term pregnancy outcome

A complicated pregnancy was defined as the occurrence of superimposed preeclampsia (initial DBP <90 mmHg with an increase of at least 25 mmHg to a DBP >90 mmHg or an initial DBP >90 mmHg with an increase of at least 15 mmHg [6], and evidence of  $\geq 300$  mg protein on 24 h urine collection or significantly increased existing proteinuria), preterm delivery (<37 weeks of gestation), and intrauterine growth restriction (birth weight <10th percentile for gestational age). Parameters of perinatal outcome included length of hospitalization in the neonatal intensive care unit and occurrence of stillbirth or postpartum death. Complications in pregnancy and the perinatal outcome were considered the short-term pregnancy outcome.

### Two year follow-up

Factors evaluated at 2 year follow-up were: maternal renal function, that is, significant increase in serum creatinine of >1 mg/dl or progression to end-stage renal disease; and infant status, namely incidence of severe handicap (cerebral palsy, blindness, deafness) or late death (as determined in a special follow-up clinic in the children's hospital affiliated with our center). A successful pregnancy outcome was defined as a live, healthy infant without severe handicap 2 years after delivery.

### Statistical analysis

We used the two-tailed Student's *t*-test and chi-square test for comparison of successful and unsuccessful pregnancy outcome in the study group. To predict pregnancy outcome on the basis of preconception and intraconception factors, stepwise logistic regression models were fitted to the data; *P* values less than 0.05 were considered significant.

Table 1. Characteristics of the study group at conception

No. of patients	38
No. of pregnancies	46
Mean age (yr) (range)*	30±4.9 (19–38)
No. of primiparas (%)	17 (37%)
No. with mild renal insufficiency (%)	34 (89%)
No. with preexisting hypertension (%)	12 (26%)

\* Results expressed as mean ± SD

Table 2. Renal function parameters of the study group throughout pregnancy (n = 38)

	Mean serum creatinine* (mg/dl)	Mean serum uric acid* (mg/dl)	Grade of proteinuria No. (%)			
			0	1	2	3
Admission trimester I + II	0.95±0.62	5.3±4.1	18 (47%)	7 (18%)	12 (32%)	1 (3%)
Trimester III	0.99±0.82	5.4±2.0	16 (42%)	8 (21%)	11 (29%)	3 (8%)

\* Results expressed as mean ± SD

Table 3. Short-term pregnancy outcome in the study group

Superimposed preeclampsia (%)	10 (22%)
Preterm delivery (%)	10 (22%)
IUGR (%)	6 (13%)
Cesarean delivery (%)	11 (24%)
Hospitalization in NICU (%)	2 (4.4%)
Stillbirths (%)	0

NICU = neonatal intensive care unit

Table 4. Long-term outcome in the study group (2 years after delivery)

Significant increase in serum creatinine (>1 mg/dl) (%)	2 (5%)
End-stage renal disease (%)	0
Severe handicap or late infant death (%)	1 (2.2%)

## Results

### Preconception parameters

Maternal characteristics at conception are presented in Table 1. Maternal age at conception ranged from 19 to 38 years (30±4.9 years) and the nulliparity rate was 37%. Renal function was normal to mildly impaired in 34 patients (89%), and preexisting hypertension was evident in only 12 (26%).

### Renal function parameters during pregnancy

No significant changes were noted in mean serum creatinine, uric acid levels, or grade of proteinuria in the study group during pregnancy [Table 2].

### Short-term pregnancy outcome

The short-term pregnancy outcome is summarized in Table 3. Pregnancy was complicated by superimposed preeclampsia in 10 patients (22%), preterm delivery also in 10 (22%), and IUGR in only 6 (13%). A higher rate of cesarean delivery (24%) than the average in our center (17%) was observed.

DBP = diastolic blood pressure

IUGR = intrauterine growth restriction

Table 5. Characteristics and short- and long-term pregnancy outcome in patients with moderate or severe renal insufficiency in the study group

No. of patients	4	
No. of pregnancies	5	
Mean age (yr) (range)	28.5±2.1	(25–30)
No. with pre-existing hypertension (%)	1	(25%)
Superimposed preeclampsia (%)	1	(25%)
Preterm delivery (%)	2	(50%)
Still births (%)	0	
Significant increase in serum creatinine (>mg/dl) (%)	1	(25%)
End-stage renal disease (%)	0	
Severe handicap or late infant death (%)	0	

## Two year outcome

At two years after delivery, renal function deterioration was observed in only two patients (5%) with primary renal disease [Table 4]. One infant in the primary renal disease group died at age 8 months due to cytomegalovirus infection.

## Pregnancy outcome in patients with moderate or severe renal failure

Four patients were classified as having moderate to severe renal failure (serum creatinine  $\geq 1.4$  mg/dl) at admission [Table 5]. Their mean age and parity were not different from the patients with mild disease. Worse short-term pregnancy outcome was observed in these patients as compared to the patients with mild disease. As for long-term outcome, renal deterioration was associated with moderate to severe renal failure in one of the two patients in the primary renal disease group.

## Prediction of outcome

In the patients with primary renal disease, uncomplicated successful pregnancy outcome (live birth without severe handicap, term delivery without the occurrence of superimposed preeclampsia or IUGR) was related to preexisting hypertension ( $P=0.01$ ) and preconception serum uric acid level ( $P=0.027$ ). Using a logistic regression model, the probability of uncomplicated successful pregnancy outcome was calculated with the formula:

$$P = e^{5.315-2.104 \cdot HT-2.844 \cdot \ln(\text{ua1})} / 1 + e^{5.315-2.104 \cdot HT-2.844 \cdot \ln(\text{ua1})}$$

where  $P$  is the probability of uncomplicated successful pregnancy outcome, HT is preexisting hypertension (1=yes, 0=no), and  $\ln(\text{ua1})$  is the natural logarithm of preconception serum uric acid in milligrams per deciliter. None of the other parameters studied, such as type of primary disease ( $P=0.16$ ), preconception and second-trimester serum creatinine level ( $P>0.1$ ), second-trimester serum uric acid level ( $P=0.18$ ), and preconception grade of proteinuria ( $P=0.054$ ), correlated with pregnancy outcome.

## Discussion

This study was performed to determine the outcome of pregnancy in women with primary renal disease. Logistic regression models were fitted to predict pregnancy outcome based on preconception and intraconception factors. We introduced new data on infant 2 year follow-up that

were not previously reported in the literature. A successful pregnancy outcome (live, healthy infant without severe handicap 2 years after delivery) was observed in 98% of the patients with primary renal disease.

Our results support the more optimistic view based on recent data [7–9] that women with underlying renal disease but with preserved or only mildly decreased renal function at conception, as demonstrated by most of our patients, usually have a successful pregnancy outcome [10]. The good pregnancy outcome observed in most of the patients with primary renal disease was mainly due to their higher incidence of only mild renal insufficiency. In addition, uncomplicated successful pregnancy outcome (i.e., no superimposed preeclampsia, IUGR or preterm delivery) was observed in 64% of the patients.

The incidence of hypertension before conception was found to be the most significant preconception parameter related to pregnancy outcome, which concurs with earlier studies [2,10,11]. Preconception serum uric acid level was also significant, and the preconception grade of proteinuria showed a borderline significance ( $P=0.054$ ). None of the other parameters studied correlated with pregnancy outcome.

Considering the immediate maternal outcome, most of the patients with primary renal disease demonstrated non-significant changes in the grade of proteinuria throughout pregnancy. The role of proteinuria in pregnancy outcome and renal function decline in patients with renal disease is controversial. Some studies have suggested that proteinuria generally does not influence pregnancy outcome or the maternal course of renal disease [7,11], whereas others maintain that additional or progressive proteinuria is detrimental to renal function [12,13]. Our results, especially the lack of correlation of proteinuria with pregnancy outcome, support the former. As for the long-term maternal outcome, significant renal function deterioration occurred only in two patients with primary renal disease (5%), although only a 2 year outcome was assessed. These results are in agreement with the main conclusion in the literature that renal disease may become clinically apparent or worse during gestation, but its natural course is probably not affected by gestation [1,7,10,14,15]. Of the 11 cesarean deliveries in the study group, 3 (27%) were performed due to severe hypertension or fetal distress, as compared with less than 10% of the indications for cesarean deliveries in the general population performed in our medical center.

In conclusion, this analysis provides useful guidelines for counseling women with primary renal disease about their prospects for a successful pregnancy and the effect of pregnancy on the underlying disease. Pregnancy in patients with primary renal disease should be undertaken only in those with mild renal insufficiency (serum creatinine  $\leq 1.4$  mg/dl), regardless of the type of disease. Blood pressure should be carefully controlled, mainly with calcium channel blockers. We do not suggest that cal-

cium channel blockers are superior to other antihypertensive drugs, but from our experience we can conclude that these drugs are safe in pregnancy. A low serum uric acid level at conception is also associated with better pregnancy outcome.

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