



# Pregnancy and Renal Transplantation

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## Abstract

**Context:** The current study aimed at providing an evidence - based and up-to-date review of the literature regarding the assessment and outcomes of pregnancy in patients with renal transplant.

**Design:** It was a review of the current literature.

**Conclusions:** According to the current study findings, the function or survival of renal allograft was not adversely affected by getting pregnant. Therefore, ideal care for these patients needs a multidisciplinary approach including maternal-fetal medicine, nephrology, and neonatology specialists.

**Keywords:** Abortion, Preeclampsia, Pregnancy, Preterm Labor, Renal Transplantation

## 1. Introduction

Although pregnancy in females with renal disease is increasingly observed, pregnancy in females undergoing dialysis is rare, and maternal and fetal morbidity and mortality are high under such circumstances (1, 2). Method of choice to treat the end - stage kidney disease and improve survival and quality of life in pregnant females with such complications is kidney transplantation (2). Restoration of pituitary - ovarian function and fertility in females is another benefit of this method (3); hence, it increases females' chance of becoming pregnant by approximately 4 - fold compared with dialysis (4-6). Murry et al., described the first cases of pregnancy in females with allograft kidney transplantation (7). According to the reported data, it is safe to get the conception 1 year after kidney transplantation (6-8). Since the function of allograft kidney, time between kidney transplantation and pregnancy, prescribed immunosuppression medication, and comorbid disease make such pregnancies risky (9), preconception counseling is needed to provide safety concerns for the mother, the infant, and the transplanted kidney.

Two major issues that arise in the first place by patients are: 1) The impact of pregnancy on transplanted kidney and 2) The outcome of pregnancy notwithstanding renal transplantation and medication intake.

## 2. Methods

The English scientific databases including Web of Science, PubMed, and Google Scholar as well as Persian databases such as SID, Magiran, and Iranmedex were searched from 1900 to 2015. The keywords searched in the current study were: [(kidney or renal) and transparent] and [pregnancy]. All papers regarding the outcomes of pregnancy patients with renal transplantation were enrolled.

## 3. Results

### 3.1. The Effect of Pregnancy on Transplanted Kidney

Although graft dysfunction and obstructive uropathy are reported in pregnant patients with kidney transplantation (9), studies compared the long - term outcomes of pregnancy on transplanted kidney with nulliparous transplanted controls did not show significant differences in the function or survival of graft in long term (10-17) (Table 1). Graft function in the 10 - year period was similar between patients with pregnancy history and controls (12-15). No significant differences are reported in the mean level of creatinine in pre- and post - pregnancy period, in many studies (12, 18-20). Rosha et al., reported no differences between the median of estimated glomerular filtration rate

(eGFR) before pregnancy and that of the time of follow - up at the last postpartum visits (17).

Serum creatinine before pregnancy could be a prognostic factor in the decline of kidney function with pregnancy as the patients with pre-pregnancy serum creatinine level  $\geq 1.7$  mg/dL had significant decline in renal function more often than the ones with normal baseline creatinine (20). As stated in the European best practice guidelines for renal transplantation, survival and graft function of such pregnant females, in the presence of normal graft function before pregnancy, is not worse (21).

**Table 1.** Graft Survival

Author	Long - term Graft Survival	Acute Rejection %
Al Duraihimh et al. (19)	Graft loss within 2 years of delivery: 0	2.9
Kashanizadeh et al. (11)	91%, at 5 - year similar to the controls	
Gorgulu et al. (12)	Similar to the controls at 10 years	
Gutierrez et al. (13)	Similar to the controls at 10 years	0.0
Kim et al. (14)	Similar to control group, 78.5% at 10th year, 67.3% at 15th year	
Pour - Reza - Gholi et al. (15)	Control group, 94.5% at 5 years and 77.1% at 10 years	6.7
Rahamimov et al. (10)	77.6% at 10 years, 61.6% at 15 years	0.0
Bouattar et al. (18)	Graft loss within 59 months: 0	0.0
Yassaee and Moshiri (22)	Graft loss over 2 years: 3.2%	2.1
Framarino et al. (23)		1.6
Pezeshki et al. (24)		11.0
Coscia et al. (NTPR) (25)	Graft loss within 2 years of delivery: 8% - 11%	
Sibanda et al. (26)	Graft loss rate during 2 years of delivery: 6%	
Ghanem et al. (9)		0.0
Di Loreto et al. (27)	Graft loss at 2 years: 0	0.0
Bramham et al. (28)		2.0
Yildirim and Uslu (29)	Graft loss within 6 months of delivery: 0	0.0

### 3.2. Fetal and Maternal Outcomes

Two important factors affecting the pregnancy outcomes are the serum creatinine level prior to pregnancy and the interval between transplantation and pregnancy. Therefore, significant associations are reported between increased risk in cesarean section rate and short interval between pregnancy and allograft transplantation ( $< 2$

years) as well as preterm delivery and high serum creatinine level ( $> 1.5$  mg/dL) before pregnancy (29).

The overall live birth rate after kidney transplantation in the US is reported higher than that of general population: 73.5% (95% CI: 72.1 - 74.9) versus 66.7% in a meta - analysis conducted on 3570 kidney transplant recipients (4). In other studies, live birth rate is reported 43.2% to 91% (Table 2).

The increased miscarriage rate after kidney transplantation is 14.0% and the rate of some adverse outcomes such as preeclampsia, preterm delivery, and delivery by cesarean section is more than that of normal population in such patients (4, 13, 24, 25).

Gestational diabetes, anemia, infection, graft dysfunction, graft pyelonephritis, de novo proteinuria  $> 1$  g/d, and obstructive uropathy are other complications affecting such pregnancies (9, 17).

It is argued that the sole independent factor to prevent severe complications is the high glomerular filtration rate (GFR) before getting pregnant (2). Accordingly, diastolic blood pressure (BP)  $> 90$  mmHg in the second and third trimesters and serum creatinine level  $> 125$   $\mu$ M/L are considered potential predictive factors for poor pregnancy outcomes (28).

### 4. Discussion

As already noted, successful pregnancy is expected in the majority of females with transplanted kidney, but maternal and fetal complication rates are high.

The most common complications are pre - eclampsia, low birth weight, and premature birth both in reports from single centers and data from large pregnancy registries. It is argued that there are some reasons for high prevalence of complications in such patients:

1. Continuation of the underlying diseases resulting in kidney transplant and their effects on pregnancy outcomes (28).
2. As mentioned above, the function of transplanted kidney before pregnancy has a great impact on pregnancy complications (2, 28, 29).
3. The immunosuppressive medications could contribute to the high pregnancy complication rate in the kidney transplanted cases (31, 32).

It was reported in some medications used by such patients that prednisone and cyclosporine can induce hypertension during pregnancy or exacerbate it and be subsequently followed by an increased risk of preeclampsia and

Table 2. Fetal Outcomes in Patients with Kidney Transplantation

Author	Country	Pregnancies	Live Births %	Abortion %	Mean Gestational Age (Weeks)	Preterm Labor%	Low Birth Weight %	Small For Gestational Age %	Gestational Diabetes %	Hypertension %	Pre-Eclampsia %	Congenital Abnormalities & Neonatal Deaths
Coscia et al. (NTPR) (25)	US	709	72.80		35-36	54	48			68	28.31	Neonatal deaths: 1% - 3%
Ievidiotis et al. (ANZDATA) (30)	Australia & New Zealand	577	76.9						1		27	
Hebral et al. (2)	France	61	83						21		26	
Sibanda et al. (26)	UK	188	79		35.6	50	54			50		Neonatal death: 0
Pour-Reza-Gholi et al. (15)	Iran	74	43.2	24.3								
Pezeshki et al. (24)	Iran	20	85.0		34.8	35	44			65	45	Neonatal death: 2
Kashanizadeh et al. (11)	Iran	86	72								5.0	
Yassaei and Moshiri (22)	Iran	95	75.8			22.1	62.5				47.4	Congenital defects: 0, Neonatal deaths: 4
Deshpande et al. (4)	US	4706	73.5	14.0		45.6			8		27	
Framarino et al. (23)	Italy	70	85.7				33.3				6.6	Hip dislocation: 1
Di Loreto et al. (27)	Italy	13	84.6		35.4	36.4					30.7	Congenital defects: 1 (Cleinfelter)
Al Duraihim et al. (19)	Multi center	234	74.4		33.2	40.8	43.1				26.1	Congenital defects: 0, Neonatal death: 4.2%
Gorgulu et al. (12)	Turkey	22				53	16				11.0	Congenital defects: 3, Neonatal deaths: 0
Kim et al. (14)	Korea	74	66		37.1	45	27				27.0	Tracheoesophageal atresia & spinal bifida: 1, Neonatal death: 1
Kwek et al. (16)	Singapore	10	100			70					50	
Gutierrez et al. (13)	Spain	30									37.0	
Bouattar et al. (18)	Morocco	10	80			25					10.0	Congenital defects: 0, Neonatal death: 0
Rocha et al. (17)	Portugal	24			35.2	54.1		33.3	8.3		25	Congenital defects: 1 (enzymatic deficit)
Bramham et al. (28)	UK	105	91		36	52	48	24	3		24	Congenital defects: 5%, Perinatal mortality: 1%
Ghanem et al. (9)	Egypt	67				40.9		19.2	5.7	19.2		Perinatal mortality: 9.6%

early delivery resulting from it (31, 32). Cyclosporine is also associated with low birth weight (25).

In a Meta - analysis, the incidence of gestational diabetes mellitus (GDM) in pregnant females with kidney transplants was 8% (4). It is assumed that diabetogenic effect of immunosuppressive drugs, especially prednisolone and tacrolimus that are used more frequently in patients with kidney transplantation, is the cause of increased incidence of GDM (2, 28).

Cardiovascular disease along with diabetes is the common comorbidity in kidney transplant recipients and both could cause a high risk pregnancy in such patients and put their allograft at risk too. Furthermore, there are some other special factors including advanced maternal age, long - term exposure to high risk pharmacological medications, and previous abdominal surgery that increase the complications of their pregnancy (4).

It is observed that in high risk population the risk of preeclampsia could be reduced by taking aspirin (33). According to the current UK guidelines, it should be advised to all pregnant females with chronic kidney disease (CKD) to take aspirin during their pregnancy (34), despite its efficacy to prevent preeclampsia, it is never studied in females with kidney transplants.

The majority of high caesarean section rates in the ones undergoing kidney transplantation is attributed to fetal distress or maternal indications and many are performed preterm.

It seems that the incidence of prematurity and low birth weight is high in such pregnancies. Majority of females with kidney transplant have children with natural development and could achieve their normal height and weight; and their performance is usually appropriate in school (35, 36).

Data on graft survival are reassuring and the range of graft loss is 0% and 8.6% at 1 year following the pregnancy (37), but the important concern is high incidence of pregnancy complications in pregnant females with kidney transplant. Investigators consistently showed that pregnancy after renal transplantation generally has excellent graft survival. In 5 studies, long-term outcomes were compared between patients with kidney transplantation and a history of pregnancy and those of nulliparous as the control and no significant differences were observed in the graft function or survival (10-14). The reported survival rates were 61.6% to 84.8% in patients with a history of pregnancy versus 58.1% to 78.8% in the controls at the 15 - year follow-up (10, 14).

## 5. Conclusions

According to the current study findings, the function or survival of renal allograft was not adversely affected by pregnancy. Despite the fact that restoration of fertility after transplantation may alter the quality of life, obstetric and perinatal complications are increased in this population. It should be considered in consultation with these patients and decision making process and post - transplantation pregnancies should be managed in a tertiary center. Therefore, ideal care for these patients needs a multidisciplinary approach including maternal - fetal medicine, nephrology, and neonatology specialists.

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