Pregnancy post Renal Transplantation

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Objectives

- Pregnancy post renal transplantation has a favorable outcome but with a price.
- Limited Sources of information.
- Literature review about maternal and fetal outcomes.
- The need for reporting and keeping registries.
- conclusions

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Letter to the Editor

Edith Helm (April 29, 1935–April 4, 2011): The World's Longest Surviving Transplant Recipient

The world's longest surviving kidney transplant recipient and the first woman in the world who successfully gave birth following transplantation, Edith Helm, has passed away in Oklahoma. She was 76 years old and died of causes not related to her renal transplant.

The successful kidney transplant procedure, the third at Brigham and Women's Hospital in Boston, was performed in May 1956 when Edith was 22 years old. Edith was the recipient of a kidney from her identical twin sister, Wanda Foster, who, following her kidney donation, also successfully gave birth four times.

Edith's transplant 55 years ago settled critical questions of pregnancy following kidney transplantation. The two previous identical twin transplants had been between males. What would happen if a female transplant patient or her donor became pregnant? Pregnancy strains a woman's healthy kidneys. After a living donated kidney transplant, both donor and recipient would be left with a single kidney, one in a normal position, the other residing in an abnormal biological natural location. Could a transplant sustain the stress of pregnancy? Our concerns were answered in 1958. Edith gave birth to a son and 2 years later a daughter with no complications. Wanda has had four healthy babies.

Based on the successful procedure in 1956, Edith's and Wanda's families have grown strong. Edith leaves her son, daughter, four grandchildren and four great-grandchildren. Wanda has 4 sons, 12 grandchildren and a 7th great-grandchild is due any day. Wanda works at the school lunchroom in Davenport, OK. Both Edith's and Wanda's family have remained a part of the extended Murray family with frequent visits together.

Risks

- Maternal
- Fetal
- Graft

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Complications from the Pregnancy

- The **mother, fetus,** and **allograft** are at risk of complications from the pregnancy.

- Maternal risks include
  - infection,
  - ectopic pregnancy,
  - gestational diabetes
  - increased likelihood of cesarean delivery.
  - hypertension and preeclampsia are common
- These conditions affect 27-38% of patients.

The newly and rapidly developing **fetus** is affected to a greater degree than the mother.

- prematurity in up to 50% of newborns,
- intrauterine growth retardation in 20% of cases
- low birth weight, immune deficiency, and perinatal infections, especially with hepatitis B virus (HBV) and cytomegalovirus (CMV).
- The incidence of congenital anomalies is reported to be similar to that in the general population

- Studies have shown that pregnancy does not appear to cause excessive or irreversible problems in the graft, if the function of the transplanted organ is stable prior to pregnancy.
- Pregnancy is known to increase glomerular filtration rates, which, in theory, could lead to hyperfiltration and glomerulosclerosis.
- However, this hyperfiltration is related to increased plasma flow with normal intraglomerular pressure; thus, no glomerular damage occurs.

Armenti (NTPR). *Clin Transpl*. 2004. 103-14.

European best practice guidelines . Section IV: *Nephrol Dial Transplant*. 2002. 17 Suppl 4:50-5.

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CHAPTER 9

Report from the National Transplantation Pregnancy Registry (NTPR): Outcomes of Pregnancy after Transplantation

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In May 1956, identical twin females were evaluated for transplantation and after a successful kidney transplant that year with one twin donating to the other, the recipient became pregnant and delivered a baby on March 10, 1958. Dr. Joseph Murray and his group (1) subsequently reported this first successful pregnancy in a transplant recipient in 1963. Further experience in this field has been gained through continued case reports, center reports, and registry data.

The National Transplantation Pregnancy Registry (NTPR) was established in 1991 to study the outcomes of pregnancies in transplant recipients in North America, including female transplant recipients who have had pregnancies and male transplant recipients who have fathered pregnancies. All pregnancy outcomes are The data also include the follow-up of parents and offspring to determine if there are any long-term effects of pregnancy for the recipient, graft or long-term sequelae for the offspring. This report reviews data collected and analyzed by the NTPR over the past 14 years. This chapter also includes 7 personal accounts of transplant recipients and their experience with a post-transplant pregnancy or in one case fathering a pregnancy. This represents the first NTPR report since the registry relocated to Temple University School of Medicine; additional entries for this year are in progress and will be reflected in future chapters.

METHODS

The study method includes a single- page question-

Table 1. Female Transplant Recipients in the United States, by Organ*

Transplanted Organ	Reported No.
Kidney	91,128
Liver	31,269
Pancreas	2,413
Kidney/Pancreas	5,578
Heart	9,831
Lung	7,295
Heart/Lung	534
Intestine	617
All Organs	148,665

*Table based on OPTN data between January 1, 1988 and October 12, 2006.

Table 2. Number of female transplant recipients who subsequently conceived*

Transplanted Organ	Recipients Who Conceived, No.	Total Pregnancies, No.
Kidney	716	1097
Liver	111	187
Liver-Kidney	4	6
Kidney/Pancreas	38	56
Heart	33	54
Lung	14	15
Heart/Lung	3	3
Total	919	1418

*Table based on data from the NTPR reported between 1991 and January 2005.

Table 3. Pregnancy outcomes in female kidney transplant recipients reported to the NTPR.

	CsA	Neoral®	tacrolimus
Maternal Factors			
Transplant to conception interval (mean)	3.3 yrs	5.2 yrs	3.3 yrs
Hypertension during pregnancy	62%	72%	58%
Diabetes during pregnancy	12%	3%	10%
Infection during pregnancy	23%	22%	34%
Rejection episode during pregnancy[1]	4%	2%	4%
Pre-eclampsia	29%	31%	29%
Mean serum creatinine (mg/dL)			
Before pregnancy	1.4	1.4	1.2
During pregnancy	1.4	1.4	1.5
After pregnancy	1.6	1.5	1.5
Graft loss within 2 yrs of delivery	11%	4%	13%
Outcomes (n)[2]	**(496)**	**(154)**	**(71)**
Therapeutic abortions	8%	1%	1%
Spontaneous abortions	12%	19%	24%
Ectopic	1%	0%	0%
Stillborn	3%	1%	3%
Livebirths	76%	79%	71%
Livebirths (n)	**(376)**	**(121)**	**(50)**
Mean gestational age	36 wks	36 wks	35 wks
Mean birthweight	2,493 gms	2,448 gms	2,378gms
Premature (<37 wks)	52%	54%	53%
Low birthweight (<2,500 gms)	46%	50%	50%
Cesarean section	51%	46%	55%
Newborn complications	41%	50%	54%
Neonatal deaths n (%) (within 30 days of birth)	3 (1%)	0	1 (2%)

[1] Rejection for CsA including chronic rejection; Neoral® and tacrolimus biopsy proven acute rejection only; [2] includes twins, triplets; CsA - Sandimmune® brand cyclosporine (321 recipients, 486 pregnancies); Neoral® brand cyclosporine (109 recipients, 146 pregnancies); tacrolimus (56 recipients, 70 pregnancies)

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Pregnancy in renal transplant recipients: the Royal Free Hospital experience

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Summary

Background: For women with end-stage renal failure of child-bearing age, renal transplantation offers a chance to start a family. Pregnancies in renal transplant recipients involve risks for graft and fetus, and need to be carefully managed.

Aim: To identify graft, fetal and maternal outcomes in our patients, and compare our results with those

and 33% of infants were small for gestational age. FGR was associated with maternal hypertension, a pre-pregnancy serum creatinine (SCr) ≥ 133 µmol/l (1.5 mg/dl), calcineurin inhibitors and the use of cardioselective β blockers. Two patients with pre-pregnancy SCr > 200 µmol/l lost their grafts within 3 years of delivery. A permanent significant decline in

48 pregnancies
in 24 RTX
recepients

26/48
pred +aza
18/48
Cyc+pred+aza
4/48
FK

Table 4 Neonatal outcomes

Neonatal outcome	RFH	NTPR 2001	UKTPR
Pre-term delivery (< 37 weeks)	56.5%	52%	49%
Mean gestational age	34.9 weeks	36 weeks	
Mean birth weight	2204 g	2493 g	
Low birth weight (< 2500 g)	50%	45%	54%
Very low birth weight (< 1500 g)	20%		18%
Fetal growth restriction	40.7%		8%
Small for gestational age (< 10^{th} percentile)	33%		

RFH, Royal Free Hospital (this study); NTPR 2001, reference1; UKTPR, reference 2.

- Our results support the observation of others that recipients should wait 1–2 years before contemplating pregnancy.

- FGR and small size for gestational age were frequent findings (FGR 41%, SGA 33%) and were associated with maternal hypertension, pre-pregnancy creatinine 133mmol/l (1.5mg/dl) and the use of calcineurin inhibitors and cardioselective b-blockers.

- We recommend that atenolol should be avoided in pregnancy and that metoprolol should not be combined with calcineurin inhibitors.

- Pregnancy appeared to have a deleterious effect on graft function in patients with pre-pregnancy serum creatinine exceeding 155mmol/l (1.75mg/dl).

- Recipients with serum creatinine >200mmol/l (2.25mg/dl) were at increased risk of graft loss. These patients should consider very carefully the risk to graft survival, if contemplating pregnancy.

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Pregnancy and Maternal Outcomes Among Kidney Transplant Recipients

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ABSTRACT

Fertility rates, pregnancy, and maternal outcomes are not well described among women with a functioning kidney transplant. Using data from the Australian and New Zealand Dialysis and Transplant Registry, we analyzed 40 yr of pregnancy-related outcomes for transplant recipients. This analysis included 444 live births reported from 577 pregnancies; the absolute but not relative fertility rate fell during these four decades. Of pregnancies achieved, 97% were beyond the first year after transplantation. The mean age at the time of pregnancy was 29 ± 5 yr. Compared with previous decades, the mean age during the last decade increased significantly to 32 yr ($P < 0.001$). The proportion of live births doubled during the last decade, whereas surgical terminations declined ($P < 0.001$). The fertility rate (or live-birth rate) for this cohort of women was 0.19 (95% confidence interval 0.17 to 0.21) relative to the Australian background population. We also matched 120 parous with 120 nulliparous women by year of transplantation, duration of transplant, age at transplantation ±5 yr, and predelivery creatinine for parous women or serum creatinine for nulliparous women; a first live birth was not associated with a poorer 20-yr graft or patient survival. Maternal complications included preeclampsia in 27% and gestational diabetes in 1%. Taken together, these data confirm that a live birth in women with a functioning graft does not have an adverse impact on graft and patient survival.

J Am Soc Nephrol 20: 2433–2440, 2009. doi: 10.1681/ASN.2008121241

- The Australian and New Zealand Dialysis and Transplant Registry.
- Analysis 40 yr of pregnancy-related outcomes for transplant recipients.
- 444 live births reported from 577 pregnancies
- the absolute but not relative fertility rate fell during these four decades.
- Of pregnancies achieved, 97% were beyond the first year after transplantation.
- The mean age at the time of pregnancy was 29 5 yr. Compared with previous decades, the mean age during the last decade increased significantly to 32 yr (P 0.001).
- The proportion of live births doubled during the last decade, whereas surgical terminations declined (P 0.001).
- The fertility rate (or live-birth rate) was 0.19 relative to the Australian background population.

- Also matched 120 parous with 120 nulliparous women by year of transplantation, duration of transplant, age at transplantation 5 yr, and predelivery creatinine for parous women or serum creatinine for nulliparous women; a first live birth was not associated with a poorer 20-yr graft or patient survival.

- Maternal complications included preeclampsia in 27% and gestational diabetes in 1%.

Data confirms that a live birth in women with a functioning graft does not have an adverse impact on graft and patient survival.

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Original Article: Clinical Investigation

Pregnancy after renal transplantation: A single-center experience

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Objectives: To examine women with renal transplants who became pregnant, and delivered at our hospital.

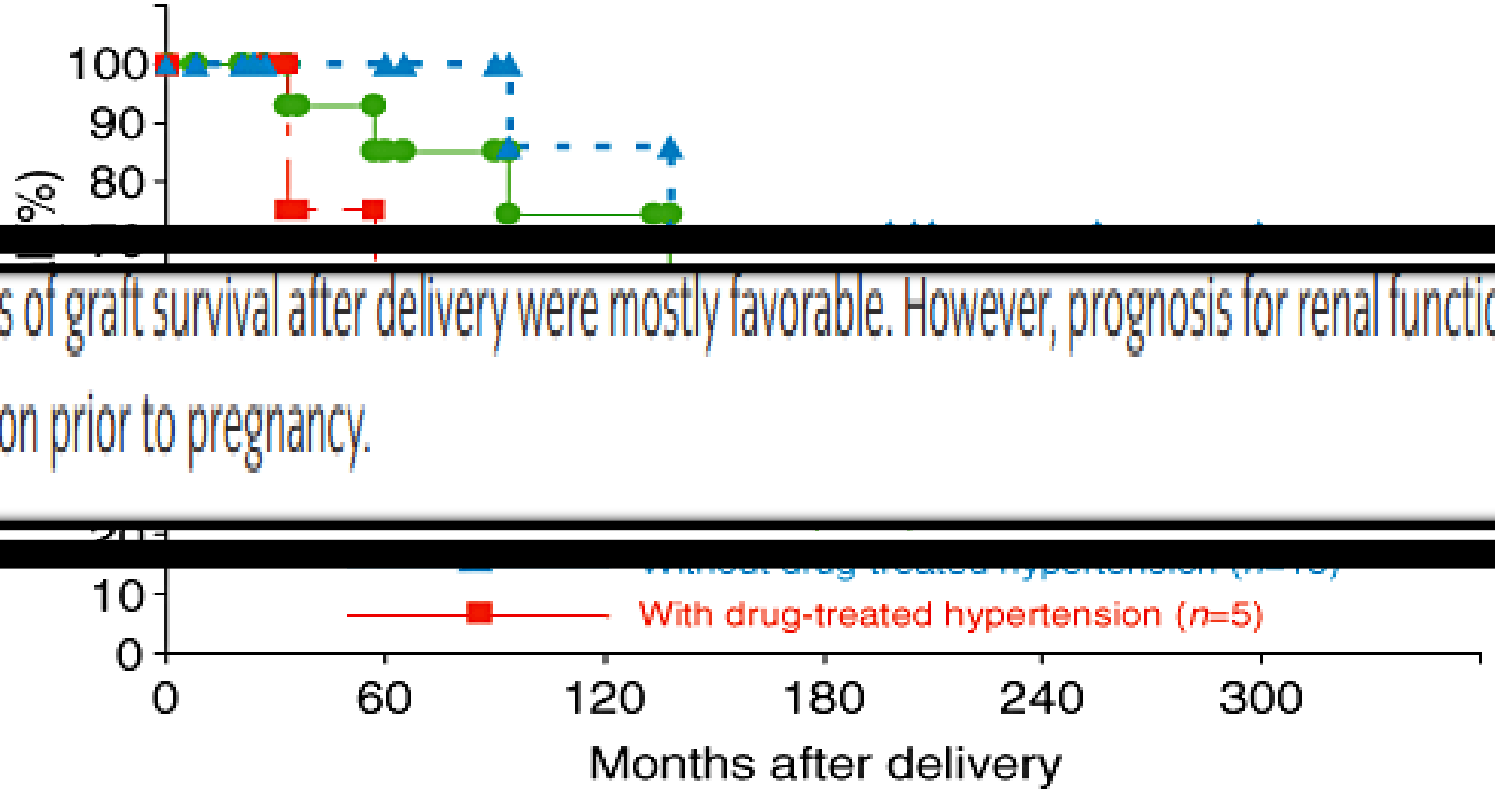
Methods: Twenty-six women who had undergone renal transplantation between 1977 and 2002 became pregnant, and delivered at Osaka University Hospital. Complete medical records of twenty of them were retrieved and retrospectively analyzed.

Results: Overall, twenty-nine pregnancies occurred in these twenty women after renal transplantation. There were spontaneous abortions in three cases, whereas pregnancy was artificially terminated five times. Thus, neonates were delivered in 21 of 29 pregnancies. One woman delivered twice and two women delivered twins. As a result, a total of 23 neonates were delivered. Mean gestational period was 35.4 weeks (range, 27–41 weeks), and mean birth weight was 2229 g (range, 724–3544 g). Regarding fetal complications, intrauterine growth retardation was observed in three cases. One child with intrauterine growth retardation died at 3 months old due to respiratory distress syndrome. One child displayed double-outlet right ventricle and another child had congenital unilateral hydronephrosis. Regarding maternal complications, prevalence of toxemia of pregnancy was 38.1%. In four of the 21 deliveries (19.0%), renal function exacerbated after delivery. Rates of graft survival for the 20 women at 1, 5 and 10 years after delivery were 100%, 85.1% and 74.4%, respectively. Prognosis for renal transplant resulted to be significantly poorer for recipients with hypertension before pregnancy than for recipients without hypertension before pregnancy (log-rank test, $P = 0.043$).

Conclusions: Rates of graft survival after delivery were mostly favorable. However, prognosis for renal function was poorer for recipients who displayed hypertension prior to pregnancy.

Key words: hypertension, immunosuppression, kidney, pregnancy, transplantation.

Pregnancy after renal transplantation: A single-center experience



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The Pregnancy Rate and Live Birth Rate in Kidney Transplant Recipients

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Background

Kidney transplantation is the preferred treatment for end-stage renal disease (ESRD). Compared to patients treated with dialysis, kidney transplant recipients live longer, have improved quality of life and consume fewer health care resources (1–3). In addition, hypothalamic gonadal dysfunction in females with ESRD may be reversed within the first few months after kidney transplantation (4). Therefore, the ability to have children is a potential benefit of kidney transplantation.

Despite thousands of successful pregnancies in kidney transplant recipients, there is limited information about the likelihood of pregnancy and anticipated fetal outcomes in these patients (4). Current data about pregnancy after kid-

- observational study of 16,195 RTx females out of 30,076 USRDS
- There were 530 pregnancies identified in 483 women
- aged 15–45 years
- 1990 and 2003
- To determine the pregnancy rate and live birth rate using Medicare claims data
- the first three posttransplant years.
- The pregnancy rate was 33 per 1000 female transplant recipients
- The live birth rate between 1990 and 2003 was 19 per 1000 female transplant recipients
- Despite a decrease in therapeutic abortions over time, the proportion of pregnancies resulting in fetal loss (45.6%) remained constant during the study due to an increase in spontaneous abortions and other causes of fetal loss.

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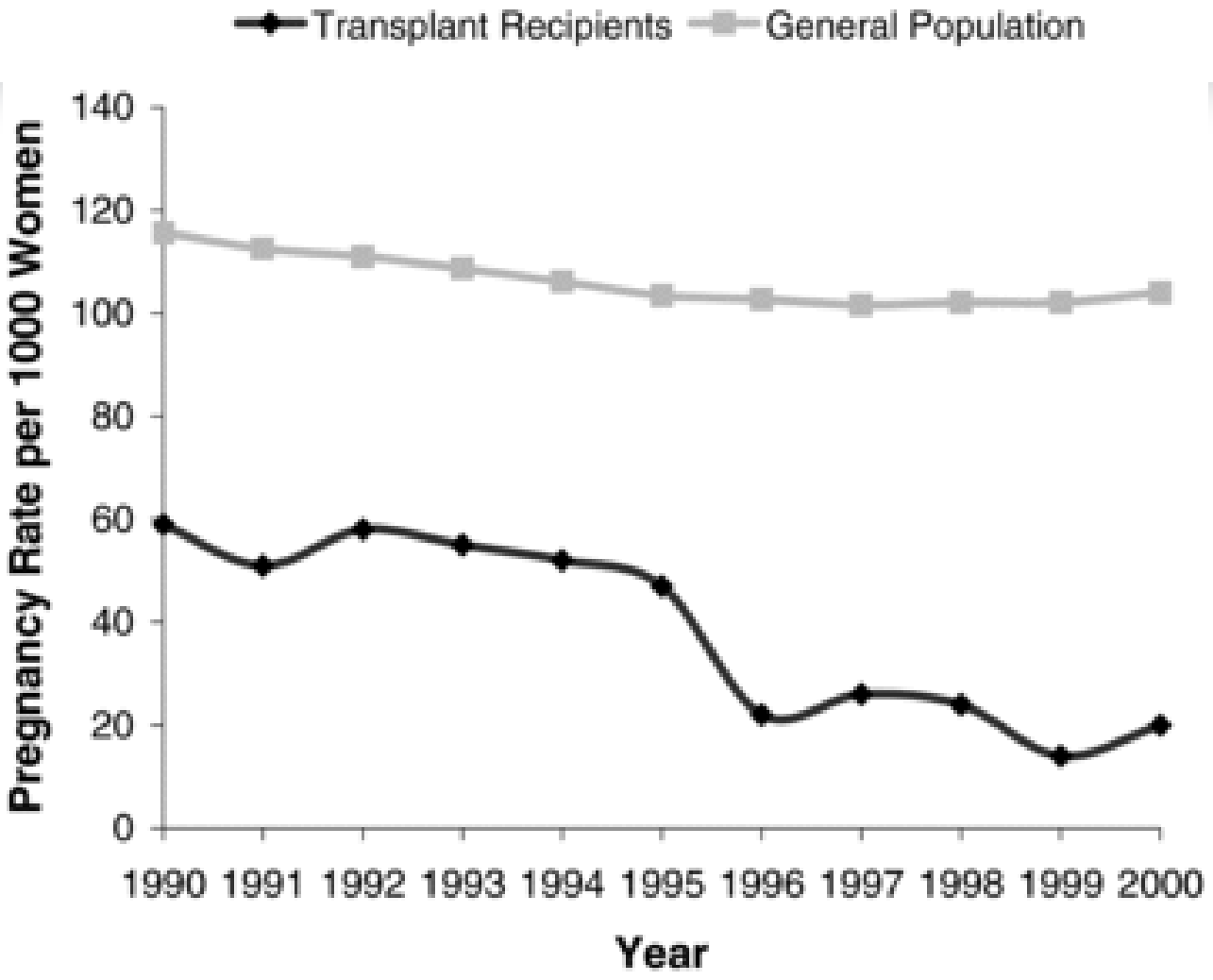
The Pregnancy Rate and Live Birth Rate in Kidney Transplant Recipients

- The pregnancy rate in kidney transplant recipients was markedly lower and declined more rapidly than reported in the general American population during the same period.



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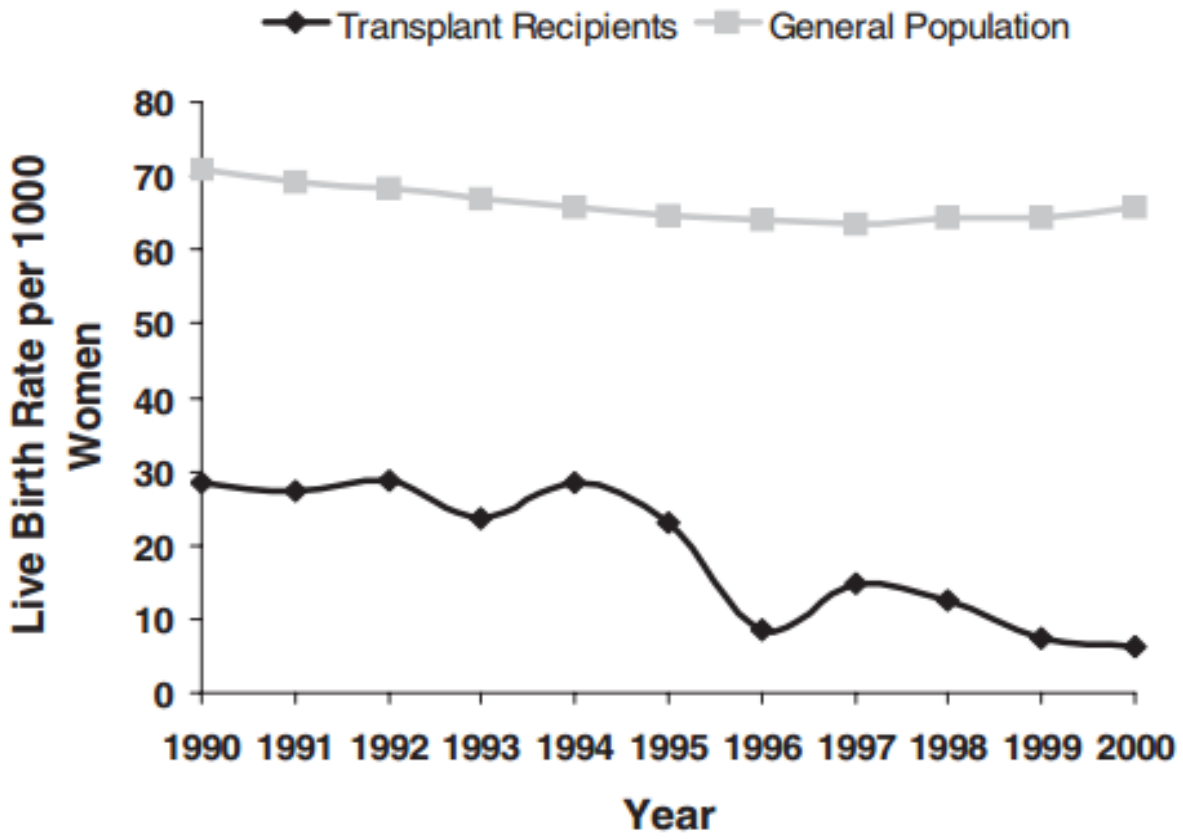
- The live birth rate was substantially lower than reported in voluntary registries of transplant recipients, and the proportion of pregnancies resulting in unexpected fetal loss increased overtime



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A Retrospective Analysis of Pregnancy Outcomes after Kidney Transplantation in a Single Center

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Key Words
Renal transplant recipient · Immunosuppression · Pregnancy

Abstract
Background: We reported pregnancy outcomes after kid-

patients had kidney rejection during pregnancy, with 2 occurring during the 6th postpartum month. ***Conclusion:*** Pregnancy should be considered a high risk in renal transplant recipients, necessitating close follow-up.

N=246 females with RTx
43 pregnancies
1982-2011
1transplant center

Table 1. Demographics of pregnant renal transplant recipients

Mean age at pregnancy, years	31.3±4.2
Mean duration of hemodialysis before transplantation, months	31.2±25.1
Mean transplantation-conception interval, months	35.9±12.6
Parity	
Nulliparous	38 (88.3%)
Multiparous	5 (11.6%)
End-stage renal disease etiology	
Unexplained	19 (44.1%)
Chronic glomerulonephritis	9 (20.9%)
Chronic pyelonephritis	3 (9.3%)
Nephrolithiasis	3 (6.9%)
Vesicourethral reflux	3 (6.9%)
Familial Mediterranean fever	2 (4.6%)
Systemic lupus erythematosus	2 (4.6%)
Alport syndrome	1 (2.3%)
Allograft source	
Live	
Living-related	12 (27.9%)
Living-unrelated	22 (51.1%)
Cadaveric	9 (20.9%)
HLA match status	
HLA match <3/6	9 (20.9%)
HLA match ≥3/6	34 (79%)
Immunosuppression protocol	
Cyclosporine-prednisolone	36 (83.7%)
Azathioprine-tacrolimus-prednisolone	6 (13.9%)
MMF-tacrolimus-prednisolone	1 (2.3%)

Table 2. Perinatal outcomes in pregnant renal transplant patients with stable graft function

Live birth rate	29/43 (67.4%)
Miscarriage rate	10/43 (23.2%)
Preterm delivery rate	7/29 (24.1%)
Preeclampsia rate	
Intrauterine growth retardation rate	
Mean creatinine level	
Prepregnancy, mg/dl	
Prenatal, mg/dl	
Postpartum, mg/dl	
Maternal anemia rate	
Transfusion rate	
Urinary tract infection rate	
Ureter injury rate	
Cesarean section rate	
Rejection rate	
Mean gestational age, weeks	30.1±6.6
Mean birth weight, g	2,407.8±874.6
Admission to intensive care unit	7/29 (24.1%)
Fetal death	1/29 (3.4%)

Table 3. Changes in pregnancy outcomes and complication rates from 1984 to 2011

	1984–1993	1994–2003	2004–2011	Total
Live birth	4	7	18	29
Miscarriage	5	3	2	10
Preterm delivery	3	2	2	7
Preeclampsia	2	1	2	5
Intrauterine growth retardation	–	1	1	2
Rejection	1	2	2	5

Successful Pregnancies in Kidney Transplant Recipients: Experience of the National Kidney Transplant Program From Uruguay

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ABSTRACT

Background. Renal transplantation increases the possibilities of pregnancy in women of reproductive age. The course of pregnancy was analyzed retrospectively in patients with kidney or kidney-pancreas transplant, surveying maternal-fetal or renal graft complications and the relation with pre-pregnancy renal function.

Table 2. Outcome According to eGFR Previous to Conception

	eGFR <50 mL/min	eGFR >50 mL/min	*P*
Gestational age (weeks)	32 ± 2	36 ± 2	.001
Birth weight (grams)	1595 ± 487	2486 ± 600	.008
Need for hemodialysis	28%	0%	.01

Table 3. Evolution of Pregnancies: Maternal and Fetal Complications

Gestations (n)	40
Live births (n)	29/40
Abortions (n)	10/40
Fetal demise (n)	1
Neonatal death (n)	1
Gestational age when born (weeks)	35 (range, 29–38)
Pre-term deliveries (n)	18/29
Ended in cesarean section (n)	28/29
Birth weight (grams)	2263 (800–3600)
LBW (n)	14/22
Pre-eclampsia/eclampsia (n)	8/30

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Pregnancy Outcomes in Kidney Transplant Recipients: A Systematic Review and Meta-Analysis

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Approximately 50 000 women of reproductive age in the United States are currently living after kidney transplantation (KT), and another 2800 undergo KT each year. Although KT improves reproductive function in women with ESRD, studies of post-KT pregnancies

Introduction

Women of childbearing age (18–49 years) with end-stage renal disease (ESRD) have fertility rates nearly 10 times lower than their healthy counterparts (1). Previous studies have suggested that kidney transplantation (KT) significantly improves reproductive function in ESRD patients, increasing fertility by approximately fourfold compared to dialysis (2–6). Fertility is restored within a few months after KT and safe conception can probably be achieved as soon as 1 year following KT (3,7). Currently, over half of the approximately 100 000 women in the United States living after KT are of childbearing age (8). Thus, preconception counseling, family planning and con-

- 50 000 women of reproductive age in the United States are currently living after kidney trans-plantation.

- Another 2800 undergo RTx each year.

- studies of post-RTx pregnancies are limited to a few voluntary registry analyses and numerous single-center reports.

- To obtain more generalizable inferences, a systematic review and meta-analysis of articles published between 2000 and 2010 that reported pregnancy-related out-comes among RTx recipients.

- Of 1343 unique studies,50 met inclusion criteria, representing **4706** pregnancies in **3570** RTx recipients.

Objectives of the metaanalysis

- The **primary goal** of this study was to systematically identify all studies of pregnancy-related outcomes in RTx recipients and estimate pooled incidences of various pregnancy events,
- obstetric complications
- delivery outcomes.
- Our **secondary goals** were to explore pre-pregnancy factors that may influence both pregnancy and graft outcomes.
- To examine the influence of pregnancy on the allograft.
- To assess recommendations for the ideal interval between RTx and pregnancy.

Table 1: Studies of pregnancy-related outcomes in KT recipients included in meta-analysis

Author (Year published)	Study years	Country	Recipients	Pregnancies
Abe et al. (2008) (17)	1977–2002	Japan	20	29
Al Duraihimh et al. (2008) (18)	1996–2006	Middle East[1]	140	234
Al-Khader et al. (2004) (19)	1984–2004	Saudi Arabia	73	113
Alfi et al. (2008) (20)	1989–2005	Saudi Arabia	12	20
Areia et al. (2009) (21)	1989–2007	Portugal	28	34
Armenti et al. (2009) (22)	1991–2009	USA	857	1356
Bar et al. (2000) (23)	1990–1995	Israel	27	42
Basaran et al. (2004) (24)	1975–2003	Turkey	8	8
Bouattar et al. (2009) (25)	1998–2007	Morocco	7	10
Cruz et al. (2007) (26)	1990–2005	Mexico	60	75
Czajkowski et al. (2004) (27)	?–2002	Poland	31	NS
Di Loreto et al. (2010) (28)	1997–2010	Italy	12	13
Diaz Gomez et al. (2008) (29)	?–2008	Spain	10	10
Fischer et al. (2005) (30)	?–2004	Germany	81	NS
Galdo et al. (2005) (31)	1982–2002	Chile	30	37
Ghafari et al. (2008) (32)	1997–2007	Iran	53	61
Ghanem et al. (2005) (33)	1984–1999	Egypt	41	67
Gill et al. (2009) (34)	1990–2003	USA	483	530
Gorgulu et al. (2010) (35)	1983–2008	Turkey	19	22
Gutierrez et al. (2005) (36)	1976–2004	Spain	35	43
Han et al. (2000) (37)	1990–1998	South Korea	14	23
Jain et al. (2004) (38)	1993–2002	USA	13	19
Kashanizadeh et al. (2007) (39)	1996–2002	Iran	86	86
Keitel et al. (2004) (40)	1977–2001	Brazil	41	44
Kim et al. (2008) (41)	1991–2005	South Korea	48	74
Kuvacic et al. (2000) (42)	1986–1996	Croatia	15	23
Levidiotis et al. (2009) (9)	1966–2005	Australia	381	577
Little et al. (2000) (43)	1985–1998	Ireland	19	29
Magee et al. (2000) (44)	1986–1996	UK	24	30
Melchor et al. (2002) (45)	1973–1998	Mexico	21	26
Miniero et al. (2002) (46)	1987–2001	Italy	42	56
Miranda et al. (2002) (47)	1976–1999	Brazil	39	47
Moon et al. (2000) (48)	?–1998	South Korea	36	48
Naqvi et al. (2006) (49)	1985–2005	Pakistan	31	47
Oliveira et al. (2007) (50)	2001–2005	Brazil	52	52
Ota et al. (2000) (51)	1990–2000	Japan	48	58
Pezeshki et al. (2004) (5)	1991–1998	Iran	50	20
Pour-Reza-Gholi et al. (2005) (52)	1984–2004	Iran	60	74
Queipo-Zaragoza et al. (2003) (53)	1980–2000	Spain	29	40
Rahamimov et al. (2006) (54)	1983–1998	Israel	39	69
Sgro et al. (2002) (55)	?–2002	Canada	44	44
Sibanda et al. (2007) (56)	1994–2001	UK	176	193
Smith et al. (2004) (57)	1980–2002	UK	20	22
Tan et al. (2002) (58)	1986–2000	Singapore	25	42
Thompson et al. (2003) (59)	1976–2001	UK	24	48
Ventura et al. (2000) (60)	1983–1999	Portugal	15	15
Wijeyaratne et al. (2000) (61)	1993–1999	Sri Lanka	10	10
Willis et al. (2000) (62)	1971–1992	Australia	48	71
Yassaee et al. (2007) (63)	1996–2001	Iran	74	95
Yildrim et al. (2005) (64)	1998–2005	Turkey	17	20

- The overall post-RTx live birth rate of 73.5% was higher than the general US population (66.7%)
- the over-all post-RTx miscarriage rate of 14.0% was lower (17.1%).
- Complications of preeclampsia (27.0% Vs 3.8%) gestational diabetes (8.0% Vs 3.9%) Cesarean section (56.9% 31.9%) and preterm delivery (45.6% Vs 12.5%) were higher than the general US population.
- Pregnancy outcomes were more favorable in studies with lower mean maternal ages.
- Obstetrical complications were higher in studies with shorter mean interval between RT and pregnancy.
- Although post-KT pregnancy is feasible, complications are relatively high and should be considered in patient counseling and clinical decision making.

ejog | European Journal of Obstetrics & Gynecology and Reproductive Biology

Pregnancy outcome after renal allograft transplantation: 15 years experience

M.E. Ghanem, L.A

A retrospective s
The study was p
Mansoura Unive

Conclusion:

Although pregnancy in renal transplant recipients is high-risk, successful outcome is expected for singleton pregnancy and is even better with repeated pregnancies in those cases with stable and good graft function. This satisfactory outcome is generally achieved if the graft is stable and the post-transplant interval is more than 2 years.

Results:

Gestational diabetes occurred in 5.7%, infection in 13.4% and proteinuric hypertension in 19.2% of pregnancies. Graft dysfunction and obstructive uropathy occurred in 30.7% and 9.6% of pregnancies, respectively, but no episodes of graft rejection were reported. Pre-term labour was found in 40.9% and fetal growth retardation occurred in 19.2% of pregnancies. Perinatal mortality was in the order of 9.6%. Pregnancy outcome was better in non-cyclosporine group, in non-proteinuric hypertensive groups and in repeated pregnancies compared to the counter groups.

Nephrol Dial Transplant (1999) 14: 846–850

Nephrology Dialysis Transplantation

Dialysis and Transplantation News

Cadaveric renal transplantation in the Kingdom of Saudi Arabia

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The development of renal transplantation in Saudi Arabia

Background

The first renal transplant operation to be carried out in the Kingdom took place in March 1979—a daughter to father donation. It was clear even then that end-stage renal failure (ESRF) was quite common in the country. Reports since then estimated it to be over 100 per million per year and in the south, where malaria and schistosomiasis are prevalent, the incidence is even higher. The Kingdom of Saudi Arabia is a vast country with an area of 2.5 million sq. km and a population of 17 million according to the 1992 census. It contains the two most sacred Mosques for Moslems all over the world, in Mecca and Medina which every able Moslem is obligated to visit at least once in his/her lifetime.

Because of the large families we have and the importance of supporting kinship that Islam directs there have been many willing donors. However, it is of interest that the majority of donations come from siblings or offspring and relatively small numbers of donors are parental, unlike the case in the West [1].

Nevertheless, it was clear from very early on that live donation was not sufficient by any stretch of the imagination, as indeed, is the case universally.

An Intermezzo—out of Country transplantation

We were determined (and still are) not to allow commercial transplantation for the well debated ethical reasons and knowing that it will kill off our live related programmes and impede the cadaveric programme.

As a result, many of our patients had to go abroad for transplantation and we received patients from many countries but the majority were from USA and India. Transplantation in USA proved costly (an average 200 000 dollars for each transplantation) and

Pregnancy post-transplantation

As part of our culture, we tend to have large families. As such, the prevalence of pregnancy post-transplantation is almost 50% in women capable of child bearing in the post-transplant population compared to only 3% in the West [33].

In our institution alone, there were 54 such pregnancies in 35 women. Our findings would suggest that with good renal function and easy to control BP, it would be safe from the mother's and baby's point of view for pregnancy to take place [34]. There is, however, an increased incidence of rise in BP, gestational diabetes mellitus and requirement to increase cyclosporin dose in the second trimester [33]. There is also an increased incidence of caesarian section and small for date babies. We have reported 17 successful pregnancies in three women [34], and found normal renal function in 22 such babies (whose mother received cyclosporin during pregnancy) after a follow up period of 43 months [35].

Nephrol Dial Transplant (1998) 13: 1281–1284

Nephrology
Dialysis
Transplantation

Case Report

Although more data is needed, we conclude from this limited information that in a well-functioning graft repeated pregnancies have no adverse effect on renal graft function and no harmful effect to the mother or

No evidence of fu ter repeated pregnancies—a re cies

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Saudi J Kidney Dis Transplant 2008;19(5):746-750

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Succes **ion**

Adnan Yaseen Alfi, M lulsalam Somro,

Nephrology Departmer dah, Saudi Arabia

Fetal Outcome (n = 20)	
Pre-term delivery (< 37 weeks)	6 (30%)
Mean gestational age	36.3 ± 3.9 weeks
Mean birth weight	2349 ± 574 gm
Low birth weight (< 2500 g)	12 (60%)
Very low birth weight (< 1500 g)	2 (10%)
Apgar Score	9-10
Fetal growth restriction	0%
all for gestational age	10%

pregnancy	
Graft dysfunction persisted (> 6 months) post-pregnancy	2 (10%)
Graft loss < 2 years post-partum	2 (10%)

ABSTRACT. To evalu female recipients who became pregnant udied 20 incident pregnancies in 12 renal related, 4 (33.3%) from deceased, and 3 (25 gnancy was 30.5 ± 4.5 years and mean inte ± 3.7 months with the interval was < 1 year in before pregnancy vs 6 months post delivery was y, ($p = 0.2$). All patients were normotensive duri hypertensive, none was markedly proteinuric, an ng one pregnancy. Graft loss one year post delive natal SCr > 132 µmol/L, and another with short interval from transplantation to pregnancy < 1 year, while the remaining 10 patients revealed current mean SCr of 105 ± 18.2 µmol/L. Complications during pregnancy included pre-eclampsia in (25%), UTI (25%), preterm delivery < 37 weeks (30%), however, none of the pregnancies ended by abortion. Normal vaginal delivery vs cesarean section was 70% vs 30%,

Outcome of 234 Pregnancies in 140 Renal Transplant Recipients From Five Middle Eastern Countries

Huda Al Duraihimh,[1] Ghormullah Ghamdi,[1] Dujana Moussa,[2] Faissal Shaheen,[3] Nabil Mohsen,[4] Usha Sharma,[4] Antoine Stephan,[5] Adnan Alfie,[6] Mohamed Alamin,[6] Mehmet Haberal,[7] Bassam Saeed,[8] Mohamed Kechrid,[9] and Abdulla Al-Sayyari[10,11]

Objective. To study the pregnancy and offspring outcomes in postrenal transplant recipients.

Methods. This is a retrospective case-note review study investigating the outcome of 234 pregnancies in 140 renal

Conclusions. In the presence of good allograft function, the majority of pregnancies in renal transplant recipients have a good outcome but with increased incidence of preeclampsia, reduced gestational age, and low birth weights. Patients with baseline serum creatinine of above 150 μmol/L have an increased risk of allograft dysfunction resulting from the pregnancy.

Keywords: Renal transplant, Pregnancy, Middle East.

(*Transplantation* 2008;85: 840–843)

TABLE 5. Maternal and fetal factors

	Using cyclosporine NTPR[a] (n=650)	UK[b] (n =193)	Our study (n=235)
Urinary tract infection (%)			19.4
Diabetes during pregnancy (%)	3–12		2.0
Rejection episode during pregnancy[a] (%)	2–4		2.95
Preeclampsia (%)	29–31		26.1
Graft loss within 2 yr of	4–11		0
Low birth weight (<2,500 g) (%)	46–50	54	43.1
Caesarean delivery (%)	46–51	64	53.4
Neonatal deaths (%)	0	0	4.2

[a] National Transplantation Pregnancy Registry (3).
[b] Transplant Pregnancy Registry (19).

What about male renal transplant recepients and any existing risks ?

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Marital Status and Fertility of 185 Male Renal Transplant Recipients in China

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HUI-MING XU,§ QI-ZHE SONG,* BIAO XU,* AND XIAN-FAN I

*From the *Center for Renal Transplantation, Jiulisong Hospital, Hangzho Transplantation Center, the Second Hospital of Shandong University, Jir Urology, the 153rd Hospital, Zhengzhou, Henan, China; and the §Zhejia Hangzhou, Zhejiang, China.*

ABSTRACT: A questionnaire was designed to assess the effects of renal transplantation in men of reproductive age on marital status and fertility. The study sought to correlate recipients' marital status and fertility with the health of the recipients after the transplantation, the health of children they fathered after the procedure, and the functioning of the transplanted kidney. Male recipients (n = 243) who were single and of reproductive age before renal transplantation were selected from 2007 recipients of a renal transplant recorded in the authors' hospitals in China. Of the 243 surveyed, 185 completed the questionnaire and participated in follow-up in the clinic or by telephone. Their marital status and fertility were investigated. Of the 185 recipients, 69 got married 12–88 months (mean, 32.19 ± 14.30 months) after renal transplantation, and 62 of 69 couples were actively attempting to become pregnant. Fifty-three patients fathered 54 children, including 1 pair of twins, 9–72 months (mean, 25.81 ± 15.33 months) after marriage. The birth weights of the newborns ranged from 2500 to 4600 g (mean, 3395 ± 456.80 g). These children developed well. Nine patients did not father any children, and 3 of thes Seven patients from chronic g after they fathe 1 child: 1 from birth of his chi birth. Our findi male recipient children, and significant eff recipients' hea It is very im contraception recipients sho the general po

Key words: Questionnaire, hemodialysis, immunosuppressive drug therapy.

J Androl 2008;29:618–621

death of 2 patients. Therefore, it is safe to conclude that the renal transplantation had no observable negative effects on the health or fertility of the male recipients, on the functioning of the transplanted kidney, or on the health of the children fathered after the procedure. The renal transplant recipients were able to produce healthy children. Unfortunately, it was difficult for us to follow

Table 4. Comparison of Contraceptives for Transplant Recipients

Contraceptive	*Advantages*	*Disadvantages*
Combined oral contraceptives	Widely available and affordable	Failure rate for typical use is 8%; estrogen-containing contraceptives may increase blood levels of corticosteroids, cyclosporine (Sandimmune), tacrolimus (Prograf), and sirolimus
Intrauterine devices	No increased risk of infection; no change in effectiveness for immunosuppressed patients; no drug interactions; does not contain estrogen	—
Intravaginal ring and combined hormonal contraceptive patch	Avoids first-pass effect; may decrease risk of drug interactions with estrogen; intravaginal ring has lower total daily dose of estrogen	Complications related to estrogen-containing contraceptives; increased circulating levels of estrogen with patch
Medroxyprogesterone (Provera)	Avoids first-pass effect; does not contain estrogen	U.S. Food and Drug Administration boxed warning for bone health combined with propensity for decreased bone mineral density
Subdermal implants	Fewer bone density effects compared with medroxyprogesterone; does not contain estrogen	—

Information from references 19 through 21.

Drugs	Category*	Maternal Effects	Fetal Effects	Breastfeeding
Prednisone	C	Immunosuppression, peptic ulcer disease, osteoporosis, pancreatitis, hypertension, aseptic necrosis of the bone, weight gain, fluid retention, glucose intolerance	May retard fetal growth and be associated with an increased incidence of low birth weight May increase risk for cleft lip	Safe
Cyclosporine (Neoral, Sandimmune)	C	Nephrotoxicity, hyperkalemia, hypomagnesemia, nausea, vomiting, diarrhea, hypertrichosis, hirsutism, gingival hyperplasia, hyperlipidemia, glucose intolerance, infection, malignancy, hyperuricemia	Growth retardation and premature birth	Avoid
Azathioprine (Imuran)	D	Leukopenia, thrombocytopenia, hepatitis, cholestasis, alopecia	Growth retardation, increased risk for congenital malformations, neonatal immunosuppression, leukopenia, and/or pancytopenia	Avoid
Mycophenolate mofetil(CellCept)	D	Thrombocytopenia and increased risk of development developing lymphomas and other malignancies, particularly	Caused fetal resorptions and malformations in pregnant rats and rabbits Data insufficient to conclude that the use of this agent during pregnancy is safe	Safety unknown
Tacrolimus (FK-506, Prograf)	C	Nephrotoxicity, hypertension, diabetes mellitus	Transient perinatal hyperkalemia, higher incidence of diabetes	Avoid
Sirolimus	C	Thrombocytopenia, leucopenia, hyperkalemia, hypomagnesemia, hyperlipidemia, hypertriglyceridemia,	Human data are limited	Safety unknown
OKT3 (Orthoclone)	C	Wheezing, difficulty in breathing, chest pain, fever, chills, nausea, vomiting, diarrhea, tremor, headache, rapid heart rate, muscle stiffness, high or low blood pressure	Effect on fetus not known; can cross placenta	Avoid

*Categories are defined as follows:

- To breast feed or NOT ??

Editorial

Pregnancy in Renal Transplant Recipients: More Questions Answered, Still More Asked

Michelle A. Josephson

Clin J Am Soc Nephrol 8: 182–183, 2013. doi: 10.2215/CJN.12131112

In this issue of *CJASN*, Bramham *et al.* identified pregnant kidney transplant recipients being managed by practitioners participating in the UK Obstetric Surveillance System, comparing their outcomes with those of a cohort consisting of two women without kidney transplants that had delivered at the same hospital just before the transplant recipients' delivery (1). This article is one of several following a 2006 published survey performed by the Women's Health Committee of the American Society of Transplantation (AST) to ascertain how pregnancies in transplant patients were managed, with the authors concluding that "Transplant recipients,

pathophysiology, these pregnancies are associated with a high rate of preeclampsia diagnoses, preterm deliveries, caesarian sections, and small for gestational age infants. In addition, the study identified prognostic factors for a poor outcome. The factors include the presence in the first trimester of a serum creatinine level >1.4 mg/dl, multiple prior kidney transplants, and presence of diastolic hypertension in the last two trimesters. Is any of this surprising or new? Not really. These findings largely overlap with results of a systematic review and meta-analysis and what has been reported to the National Transplant Pregnancy Regis-

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- With the ever-changing immunosuppression strategies, we will always question the effect of new medications on the developing fetus.

A current case is belatacept, which is a US Food and Drug Administration pregnancy category C drug. There are no human studies that provide pregnancy safety data.

- Even if immunosuppression were no longer a consideration (if we ever achieve tolerance in transplantation), we will then wonder whether pregnancy could affect that immunologic tolerant state.

- There is also a question of whether a female kidney donor adds risks to her own future pregnancies.

- We still lack prospective data despite a proliferation of large pregnancy trial networks in which accruing such data are possible.

- it is important for the transplant community to support registries like the NTPR.

- We need to advise our patients to contact NTPR and report on their outcomes (both good and bad).
- The registry serves many important roles, including being able to detect and document changing trends in pregnancy outcomes, and may provide clues when unanticipated problems arise with immunosuppressive medications.
- Pregnancy in transplant recipients is a glass more half full than half empty or vice versa ????.
- We are now in a better position to inform and counsel your kidney transplant patients and their partners and help them consider their options and decide if pregnancy and its potential risks is a journey they wish to take.

DIAVERUM

factors that favor a good outcome of pregnancy

- Serum creatinine level less than 1.5 mg/dL
- No recent episodes of acute rejection
- Blood pressure within the reference range
- Proteinuria level less than 500 mg/d
- Maintenance level of immunosuppression
- Normal appearance of allograft ultrasonography

Conclusions

- The post RTx pregnancy is a high-risk classification of pregnancies.
- Special attention should be given to obstetric complications such as hypertension, preeclampsia, gestational diabetes.
- as well as delivery outcomes such as Cesarean section and preterm delivery.
- RTx recipients tend to deliver preterm and low birth weight babies.
- Subsequent risk for adult diseases
- multidisciplinary team to be involved in the management
- Continuous reporting as case histories or and registries especially in view of the new IS medication
- Counseling of RTx recipients and partners both before and during pregnancy

Thank you

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