Renal Transplantation and Pregnancy

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Abstract

Objective: The aim of this study is to evaluate maternal & fetal outcome in cases of renal transplant patients.

Methods: This is a retrospective study from 2010 to 2012 at a tertiary care centre. We analyzed six pregnancies in five renal transplant recipients for maternal and fetal outcome in terms of clinical and biological data.

Results: The mean age was 28.6 ± 3 years. The mean time interval between renal transplantation and pregnancy was 2 year & 7months. Regarding the immunosuppressive therapy all patients received steroids, three patients received Tacrolimus, one patient received Sirolimus and Mycophenolate Mofetil that was changed 1 month before conception. There was no significant difference between the serum creatinine levels before and during pregnancy. Amongst the five patients, two of them had pre -existing hypertension. Of these two patients, one developed super imposed pre-eclampsia. The other complications which were noted were urinary tract infection in one case, premature labour pain in one case, anaemia in two cases. No neonatal complication except low birth weight was noted. Two cases had spontaneous abortion. Caesarean section was performed in two cases due to severe oligohydroaminos.

Conclusion: Pregnancy in renal transplant patient can be continued under optimal circumstances, including stable allograft function for at least 1 year post transplant without rejection with good control of blood pressure, and after appropriate adjustment of immunosuppressant and other known teratogenic medications prior to conception.

Keywords: pregnancy, renal transplant, immunosuppressive therapy.

INTRODUCTION

As fertility can be restored to normal soon after renal transplant, it is important for physicians caring for recipients to inform the patient about the potential risks of pregnancy. Pregnant recipients should be managed in close conjunction with a nephrologist. It is important to recognize that regular menses and fertility are usually restored shortly after successful transplantation and has been reported as early as 3 weeks post-transplant (1,2). In a study data of United States Renal Data System (USRDS), from 1990 to 2003, Gill et al. estimated a pregnancy rate of 33 per thousand (3.3%) in female kidney transplant recipients of child bearing age in the first 3 years post-transplant (3). Of these pregnancies, only 55.4% ended in a live birth. In contrast, the National Transplantation Pregnancy Registry (NTPR) and the UK transplant pregnancy registry reported much higher live birth rates of 75-80 %. In the USRDS data the outcomes of spontaneous and therapeutic abortion were 21.2% and 3.8% respectively (3).

Criteria for considering pregnancy in renal transplanted patients include good post-transplant health for 2 years, stable allograft function with a serum creatinine < 1.5 mg/dl, absence of rejection, control of blood pressure, absence of proteinuria (<0.50 g/dl), and normal allograft ultrasound. All of the medications used in post-transplant immunosuppressive regimens cross the placenta and expose the foetus to potential toxicities (4,5). Effect of these medications on the foetus is difficult to determine because of the lack of controlled trials on drug safety in pregnancy (4). Pre-existing kidney disease is an independent risk factor for preeclampsia, diabetes mellitus, various opportunistic infections, anemia, prematurity, low birth weight, and neonatal death (6, 7). Safety of breastfeeding by mothers receiving immunosuppressant remains uncertain because of passage of medications into breast milk and the unknown neonatal exposure. The aim of this study is to evaluate maternal & fetal outcome in cases of renal transplant patients.

MATERIAL & METHODS

This is a retrospective study from 2010 to 2012 at a tertiary care centre. We analyzed 6 pregnancies in 5 renal transplant recipients. The studied parameters included transplantation-pregnancy interval, presence of hypertension prior to pregnancy, new onset hypertension, worsening hypertension, new onset proteinuria, urinary tract infection, gestational age, and mode of delivery, foetal outcome, renal graft function before, during and after pregnancy, and immunosuppressive toxicities. During the pregnancy patients were examined monthly in renal transplant outpatient department to monitor arterial hypertension, serum creatinine, complete blood count, proteinuria, side effects of immunosuppressive drugs and treatment.

RESULTS

In our study, the mean age was 28.6±3 years. The mean time interval between renal transplantation & pregnancy was 2 years & 7months.All patients had stable allograft function with absence of rejection, normal allograft ultrasound absence of proteinuria.

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Table 1: Demographic Features						
Case	1	2	3	4	5	6
Age(years)	28	30	26	28	31	30
Date of Tx	05/12/07	19/07/11	23/11/07	19/11/08	22/03/08	05/12/07
Type of Tx	protocol	Control	protocol	protocol	cadaver	protocol
Donor relation	father	Father	Husband	mother	cadaver	father
HLA match	3/6	3/6	0/6	3/6	-	3/6
Basic disease	CGN CKD	CGN CKD	VUR CKD	CGN CKD	PIH CKD	CGN CKD
Year of pregnancy	Feb 2010	Nov 2012	Jan 2011	June 2012	Mar 2012	Nov 2012
Duration of pregnancy	9 month	2 month	3 month	9 month	8 month	6week
*First patient conceived for the second time in November 2012 and opted for MTP at 6 week. #CGN(Chronic glomerulonephritis), Vesicoureteral reflux (VUR) ,Pregnancy induced hypertension(PIH)						

Regarding immunosuppressive therapy , all patients received steroids , three patients received Tacrolimus, 1 patient received Sirolimus & Mycophenolate mofetil that was changed 1 month before conception. There was no significant difference between the serum creatinine levels before and during pregnancy. Two patients had hypertension before pregnancy which was controlled by anti-hypertensive drugs, amongst them one patient developed super-imposed pre-eclampsia controlled with Tablet Nifedipine retard 20mg TDS and Tablet Alpha-methyl dopa 500mg QID .

Anaemia was noted in two cases, urinary tract infection in one case & pre-term labour developed in one patient (who delivered at 32 weeks by vaginal route). Two cases had spontaneous abortion. Caesarean section was performed in two cases in view of severe oligohydroamnios. One patient conceived twice but opted for termination of second pregnancy at 6 week of gestation in view of health & economic status. No neonatal complications except low birth weight were noted.

DISCUSSION

Pregnancy after kidney transplantation is a better option for female recipients of child bearing age who wish to have a family. During pregnancy it is important to pay close attention to medical complications such as worsening of hypertension and development of preeclampsia, risk of opportunistic infection, and worsening of anemia.

Mycophenolic acid is contraindicated during pregnancy. Sirolimus should be avoided during pregnancy. Drugs that can be used during pregnancy are steroids, Azathioprine, Cyclosporine and Tacrolimus. Frequent monitoring of Tacrolimus and Cyclosporine is required. Breast feeding is avoided for drugs except steroid. Biopsy can be done during acute reaction. Vaginal delivery is preferred, while caesarean delivery is indicated only for obstetrical reasons. .Mycophenolic acid (MPA) products have been reported to cause various deformities such as hypoplastic nails, shortened fifth fingers, and ear and facial deformities (8, 9, and 10). MPA products and Sirolimus are to be avoided and discontinued 6 weeks prior to a planned pregnancy (11, 12, and 13).

Hypertension and Preeclampsia developed in 50% of pregnant renal transplant recipients compared to

Table 2: Pre-Pregnancy Status						
	CASE 1	CASE 2	CASE 3	CASE4	CASE 5	CASE 6
S.creat	1-1.1	0.8-1.0	1.1-1.2	0.8-1.0	0.8 – 1.0	1-1.1
Urine protein	Nil	Nil	Nil	Nil	Nil	Nil
Maternal infection	No	No	HCV+	No	No	No
Antihypertensives	NFR20BD Dilzem SR	No	No	No	Amlo 5 OD	NFR20BD DilzemSR
Immunosupressants	Pred 10 Tacro 1mg BD	Pred 10 Siro 1 OD	Pred 10 Tacro 1 mg BD	Pred 10 MMF 360 TDS	Pred 10 Tacro 0.5 OD	Pred 10 Tacro 1mg BD
Graft Doppler	WNL	WNL	WNL	WNL	WNL	WNL
General condition	Good	Good	Good	Good	Good	Good
#NifedipineRetard(NFR),Amlodipine(Amlo),Prednisolone(Pred),Tacrolimus(Tacro) ,Sirolimus(Siro), Mycophenolate mofetil (MMF)						

Table 3: Maternal Complications & Outcome						
	CASE 1	CASE 2	CASE 3	CASE4	CASE 5	CASE 6
Hypertension	Yes	No	No	No	Yes	Yes
Pre-eclampsia	Yes	No	No	No	No	No
UTI	No	No	No	Yes	No	No
Anaemia	Yes	No	No	No	Yes	No
Pre-term labour	No	No	No	No	Yes	No
Immunosuppressant	Pred 10 Tacro 1mg BD	Pred	Pred 10 Tacro	Pred	Pred 10 Tacro	Pred 10 Tacro 1mg BD
Anti- hypertensive	NF-R 20QID M dopa QID	No	No	No	M dopa QID	M dopa QID
Type of delivery	LSCS	Spontaneous abortion	Spontaneous abortion	LSCS	Pre-term delivery	MTP
Recurrence of disease	No	No	No	No	No	No

only 5-8% in general population (8, 11 and 14). Alpha methyl dopa is considered the drug of choice because of its well documented safety and lack of teratogenicity. Caesarean section was performed in 28.5% patient. The high rate of caesarean section may be explained by obstetrical indications or the fact that it is a precious pregnancy. If a caesarean delivery is performed, attention should be paid to the course of the transplanted ureter, which runs between the transplanted kidney and the bladder.

CONCLUSION

Pregnancy in a renal transplant recipient is high risk and should be co-managed by a high risk obstetrician, specifically one with experience in caring for patients with renal dysfunction (11, 15). Pregnancy in renal transplanted patient can be carried out under optimal circumstances, including stable allograft function for at least 1 year post transplant without rejection, good control of blood pressure, and appropriate adjustment of immunosuppressant and other known teratogenic medications prior to conception. With close medical and obstetric follow up, successful outcome for both the mother and the infant is possible. Patient to be counseled and to be given best available information about conception and child bearing in these cases, there is fifty percent chance that mother will be dead before the child celebrates 15th birthday. ■

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