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Pregnancy after Renal Transplantation

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SUMMARY

From October of 1986 to December 1993, 240 patients (167 male and 73 female) with end stage renal disease entered renal replacement therapy programme at Shaikh Zayed Hospital, Lahore. Renal transplantation was successfully carried out in 97 patients (76 male and 21 female). Out of 21 female patients with renal transplants 2 were menopausal and 2 were unmarried. Pregnancy was theoretically possible in remaining 17 females with age range 26-45 years having normal menstrual cycles. We report 4 successful pregnancies which occured in 3 of our transplanted patients. Immunosuppression was continued as before. No significant adverse fetal effects were noted. No mother had pre-eclamptic toxaemia or significant problem with graft function. We conclude that in normally menstruating renal transplant recipients who are desirous of having babies, successful pregnancy is possible and can be allowed to continue under strict follow up provided they have good functioning grafts and controllable or no hypertension. This is probably the first report of its kind from our country.

INTRODUCTION

Infertility invariably accompanies renal disease when serum creatinine is more than 2 mg/dl. Even if pregnancy occurs, its effects on remaining renal function are adverse (especially in the presence of hypertension) at the same time the out come of gestation is uncertain[1]. The reported conception rates are less than 1 per 200 in patients with end stage renal disease[2]. However, fertility improves after successful renal transplantation[3]. First successful delivery after renal transplantation was reported in 1963[4]. Ever since more than 2000 pregnancies have been reported in the literature in renal allograft recipients population[5]. It is estimated that about 1 in 50 women of child bearing age with a good functioning renal transplant becomes pregnant[6]. Since the number of patients undergoing renal transplantation is increasing the number of long term survivors growing, more pregnancies will occur. This article describes our experience of dealing with three patients with good functioning renal grafts, who became pregnant and were followed up during pregnancy labour and subsequently at our institution.

Purpose of the study

To study the outcome of pregnancy in patients with renal transplants and to determine the effects of gestation on the well being of the mother and the new born.

PATIENTS AND METHODS

During the period from October 1986 to December 1992, a total of 240 patients (167 male and 73 female) with end stage renal failure entered renal replacement programme at Shaikh Zayed Hospital, Lahore. Ninety two patients underevent successful renal transplantation from living donors (71 male and 21 female). Out of these 21 female renal transplant, recipient pregnancy was possible in 17 and out of these 3 became pregnant with 2 consecutive pregnancies in one patient. These 3 women had regular menstrual cycles restored, after transplantation, but were advised not to have conception for 1½ years (Table 1). Original renal disease was chronic GN in 1, chronic pyelonephritis in 1 and one patient had reflux nephropathy. 2 out of these 3 patients were also hypertensive. Renal transplantion was done 10-24 months (mean 19

months) prior to becoming pregnant from living donors (2 related and one unrelated) (Table 2).

Table 1: Age groups and fertility in transplanted females.

Age groups	*No. of Pt.*	*Unmarried*	*Menopausal*
< 20 yrs	2	2	-
21-30 yrs	6	-	-
31-40 yrs	11	-	-
41-50 yrs	1	-	1
> 50 yrs	1	-	1
Total	**21**	**2**	**2**

All the patients were getting drugs for immunosuppression regularly. Predinsolone 0.16kg/day. Azathioprine 2 mg/kg/day and cyclosporin 2 mg/kg/day. Antihypertensive therapy was continued in 2 patients. On reporting amenorrhoea pregnancy was confirmed by pregnancy test and ultrasonography and the patients were advised to consult gynaecologist at fortnightly intervals upto 36 weeks and then on weekly basis. Blood pressure, weight gain and fetal well being was monitored alongwith assessment of renal function. CBC, urinanlysis, urea creatinine and serum electrolyte estimation was done on each visit.

The outcome of pregnancy was studied as well as harmful effects on the fetus and the mother were noted.

RESULTS AND OBSTRUCTION

Out of 21 female patients with renal transplants, two women were menopausal and 2 were unmarried. Out of remaining 17 patients 3 became pregnant and 4 successful pregnancies resulted (Two consecutive pregnancies in one). Their mean age was 27 years and they had stable renal function and controllable hypertension. Immunosuppression and antihypertensive therapy was continued throughout gestation.

The antenatal data showed a mean weight gain of 8.6 kg by each mother and mean gestational age was 37 weeks. Two deliveries were spontaneous vaginal deliveries with episiotomies, the third was a Forceps delivery with perineal tear. Fourth was a caesarean section done due to fetal distress and premature rupture of membranes (Table 3).

Three issues were males and one female. Mean birth weight was 3.14 kg with mean apgar score of 7/10. The babies had no evidence of congenital malformation and except pneumonia in one and jaundice in the other (which improved with treatment), there was no perinatal problems (Table 4).

DISCUSSION

End stage kidney disease and female sexual functions

Pregnancy in women with moderate to severe kidney disease is a rarity. Menstrual disturbances are frequently seen when the glomerular filteration rate falls to 10 ml/min. Maintainence dialysis may restore menstruation but infertility remains high. With end stage kidney failure, there is loss of libido and the menstrual cycles are anovulatory. It has been shown that the normal midcycle surge of FSH and LH which precedes ovulation is usually absent or not followed by rise in progesterone concentration[7]. Moreover elevated prolactin concentrations are commonly observed in patients undergoing haemodialysis[8].

Pregnancy after renal transplantation

Successful kidney transplantation usually results in reappearance of menstruation and return of normal sexual function[9]. Patients are advised not to have pregnancy for at least 1½ years after renal transplantation.

The suggested criteria for pregnancy in transplanted patients are[5].

1. Good health.
2. Stable renal function for 1½ years after transplantation.
3. Stature compatable with good obstetrical outcome.
4. Absent or minimal proteinuria.
5. No or easily controlled blood pressure.
6. No evidence of obstructive uropathy.
7. Serum creatinine less than 2 mg/dl, preferrably less than 1.4 mg/dl.
8. Lowest possible dose of immunosuppressive therapy.
   - Predenisolone 15 mg/day or less
   - Azathioprine 2 mg/kg/day or less
   - Cyclosporine - A 2-4 mg/kg/day or less.

Table 2: Data of patients who conceived.

	Age	*Diagnosis*	*Peroid with transplant*	*Type of graft*	*Medication*
Case 1	26 yrs	Chronic GN Hypertension	2 yrs	Live related	Prednisolone Azathioprine Cyclosporin A Methyldopa
Case 2	28 yrs	Ch. pyelo-nephritis hypertension	10 months	Live unrelated	Prednisolone Azathioprin Cyclosporin A Atenolol
Case 3	27 yrs	Reflux Nephropathy	2 yrs	Live related	Prednisolone Azathioprine Cyclosporin A

Table 3: Near term maternal antenatal data.

	No. of prenancies	*Blood pressure (mmHg)*	*Weight gain (Kg)*	*Duration of pregnancy (wks)*	*Mode of delivery*
Case 1	$G_1P_0A_0$	130/90	10	38	SVD with episitomy
Case 2	$G_3P_2A_0$	130/90	7	34	Emergency C. Section
Case 3	$G_2P_0A_1$	130/80	8.5	39	Forceps
	$G_3P_1A_1$	140/80	9	37	SVD with episotomy

Table 4: Obstetrical outcome

Case No.	*Gestational age (wks)*	*Sex of baby*	*Birth weight (kg)*	*Apgar score*	*Congenital anomalies*	*Perinatal course*	*Treatment*
1.	38	Male	3.2	8/10	None	Uneventful	None
2.	34	Female	2.2	5/10	None	Chest infection Aspiration pneumonia	Intubation Resuscitation Antibiotics
3.	39	Male	3.5	7/10	None	Uneventful	
	37	Male	3.75	8/10	None	Jaundice	Phototherapy

Each pregnant renal transplant recipient should be monitored carefully by a nephrologist and obstetrician on biweekly intervals upto 36 weeks and then weekly. Patient's blood pressure, weight, gestational size, well being, and other renal biochemical parameters should be checked side by side. Mean values in our patients are shown in Table 5.

Data on 115 pregnancies which occurred in renal transplanted patients was published in 1980 by registration committee of the European Dialysis and Transplant Association[10]. Fifty four patients had spontaneous abortion, 45 therapeutic abortions, and out of remaining 16, only 12 were completed. Mean birth weight was 1900 gms. Dr Davison[11] surveyed

Table 5: Biochemical data of mother and newborn (mean values).

	Hb (gm/dl)	*TLC 10^9/l*	*Platelets /cmm*	*Urine M/S*	*Serum Na^+ mmol/l*	*Serum K^+ mmol/l*	*Serum Cl^+ mmol/l*	*Serum Bilirubin mmol/l*	*SGPT IU/l*	*SGOT IU/l*	*Alk. Phos IU/l*
Case 1											
Mother	11.0	9.4	185,000	WBC 1-2	136	3.8	98	0.8	26	24	346
Newborn	16.2	12.4	300,000	RBC 1-2	-	-	-	1.4	-	-	-
Case 2											
Mother	13	9.8	270,000	WBC 3-4 RBC + +	145	3.9	107	2.0	23	48	367
Newborn	10.8	10.8		-	-	-	-	3.8	52	52	483
Case 3											
Mother	9.7	17.0	245,000	WBC 10-15 RBC + +	140	4.2	102	1.0	34	32	450
Newborn	18.2	16.0	250,000	-	-	-	-	-	-	-	-
Mother	10.2	12,000	200,000	WBC 6-8 RBC + +	138	4.0	100	1-2	3.4	38	390
Newborn	16.4	15.4	290,000	-	-	-	-	10.6	38	42	116

2309 gestation in 1594 allograft recipients and noted that 40% of pregnancies could not complete 1st trimester. Out of remaining 60% who had serum creatinine < 1.5 mg/dl success rate of pregnancy was 90% but with higher serum creatinine values success rate decreased to 60%. It is therefore suggested that all patients should be taken as high risk because of a host of complications in both fetus and further due to immunosuppression[12].

In our study, the number of patients included is very small and no clear conclusions can be drawn regarding outcome of pregnancy in female transplant recipients but this is probably, one of the preliminary reports of pregnancies in transplant patients and first from our institution.

Labour and delivery

Transplanted kidney which is located in the false pelvis, poses no mechanical problem to normal vaginal delivery. None of our patients had such problems. Two had normal vaginal deliveries and one had emergency caeserian section due to fetal distress and ruptured membranes. Mothers received supplemental steroids for the stress of labour.

Risk to fetus

Apart from mother there are multiple risks to which the fetus is exposed e.g. prematurity, low birth weight, lymphopenia, septicemia, adrenal suppression, respiratory distress syndrome and neonatal sepsis. Immunosuppression also causes congenital defects and chromosomal abbreviations.

One of our newborns had aspiration pneumonia necessitating endo-tracheal intubation and use of antibiotics. One new born had jaundice which was attributed to hepatic prematurity and improved with phototherapy alone. Intraterine growth retardation is a frequently reported observation[13,14]. The immaturity is mainly thought to be due to cyclosporine and immunosuppressive drugs[15]. Birth defects have been reported in off-springs of male recipients of kidney[16]. None of our patients had any detectable congenital abnormality at birth, though the birth weight was low, 2.2 kg, at 34 weeks in one, and 3.75 kg at 37 weeks delivery in the other.

Mothers were advised not to breast feed their babies.

Risk to mother

Renal function impairement has been described during pregnancy in patients with pre-existing renal impairment[17]. Davison has also showns that renal allograft adapt to pregnancy normally and that decrease in GFR and proteinuria occurs in the third trimester commonly but is usually transient[18]. Some renal impairment did occur in one of out-patients and her creatine rose from 1 mg to 1.4 mg/dl during pregnancy (Table 6).

The reported risk of pre-eclamptic toxaemia is 27% in renal transplant patients with pregnancy[10]. All our patients had a smooth course and blood pressure control was not a problem.

Table 6: Laboratory data (mother).

	Pre-pregnancy	*During pregnancy*	*After pregnancy*
Proteinuria			
Case 1	Trace	Trace	Trace
Case 2	Nil	Trace	Nil
Case 3	Trace	Trace	Trace
Blood urea			
Case 1	24 mg/dl	20 mg/dl	30 mg/dl
Case 2	30 mg/dl	26 mg/dl	26 mg/dl
Case 3	36 mg/dl	40 mg/dl	32 mg/dl
S. Creatine			
Case 1	1.4 mg/dl	1.0 mg/dl	1.2 mg/dl
Case 2	1.0 mg/dl	1.4 mg/dl	1.3 mg/dl
Case 3	1.3 mg/dl	1.1 mg/dl	1.4 mg/dl

CONCLUSION

Pregnancy in renal transplant patients can be allowed to take place, if the renal function is good and the dose of immuno-suppression is minimal and there is no or controllable hypertension. Strict follow up with good blood pressure control results in a favourable outcome of pregnancy without having significant adverse effects to either mother or fetus.

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