An Overview on Fertility Outcome in Renal Transplant Recipients

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Abstract

Background The number of patients undergoing renal transplant are increasing with time. Most of these patients fall in the reproductive age group, who are going to conceive sooner or later. But there are few recipients who either are infertile before transplant or became infertile due to underlying renal pathology responsible for transplantation.

Objective To study fertility outcome in female renal transplant recipients.

Materials and Methods Study design: This is a retrospective study conducted at tertiary health center in Ahmedabad, from 2004 to 2014. Inclusion criteria: Renal transplant recipients in the reproductive age group (20–40 years of age) were followed up in gynecology outdoor patient department. Sample size: There were 211 female renal transplant recipients, out of which 113 (53.5 %) patients had complete family, 3 (1.41 %) patients were infertile, 16 (7.58 %) patients have conceived, 33 (15.63 %) patients were lost to follow-up and remaining 46 (21.8 %) did not try for pregnancy. Exclusion criteria: Unmarried patients, divorced and widow patients were excluded.

Results Out of 19 patients, 16 patients conceived and 3 were infertile. The main cause of infertility in these patients was ovarian factor in 2 patients and tubal factor in 1 patient. Among 16 patients, 8 patients had missed abortion, 2 patients had preterm deliveries and 6 patients had term deliveries.

Conclusion Peritransplant and preconceptional counseling plays an important role for renal transplant recipients to help them understand the effect of renal pathology and transplantation on their fertility. They can have good fertility and pregnancy outcome with optimum functioning graft.

Keywords Renal transplant recipients · Infertility · Peritransplant counseling

Introduction

Patients with end-stage renal disorder can have sexual dysfunction and infertility, due to endocrine aberrations, vasomotor dysfunction, drugs or psychological factors [1]. Sexual dysfunction improves following transplant [1, 2]. These patients have good fertility outcome, except few who remain or become infertile following transplantation. These patients are at high risk of developing gestational hypertension, preeclampsia, premature rupture of membranes and even graft rejection during their antenatal period [3]. But these complications can be prevented and managed by

proper peritransplant and preconceptional counseling along with optimal graft function.

Materials and Methods

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Exclusion Criteria

Unmarried patients, divorced and widow patients were excluded.

Results

Out of 19 renal transplant recipients, 16 patients conceived and 3 were infertile. The mean age of patients was 32 ± 4.28 years. The most common cause of renal transplant was crescentic glomerulonephritis (68 %) followed by other causes (Fig. 1).

Fig. 1 Causes of renal transplantation

Table 1 Classification of prepregnancy s.cr (in mg/dl) and fertility outcome

	<1.2 (<i>N</i> = 9)	≥1.2 (<i>N</i> = 10)	<i>P</i> value
Abortion	2 (22.22 %)	6 (60 %)	0.17 (NS)
Delivery	6 (66.67 %)	2 (20 %)	0.07 (NS)
Infertility	1 (11.11 %)	2 (20 %)	1.00 (NS)

All collected data entered into the SPSS V20 and analysis has been conducted

Non-continuous data are countable and are expressed as percentages or numbers

Fisher's exact test has been used for carrying out the statistically significant value, i.e., *P* value

Table 2 Infertility in female renal transplant recipients

	Case 1 (29 years)	Case 2 (35 years)	Case 3 (30 years)
Type of infertility	Secondary with previous history of 1 abortion	Primary	Primary
Duration of infertility (years)	5	11	5
Cause of infertility	Ovarian factor	Tubal block ^a	Premature ovarian failure
Cause of transplant	Crescentic glomerulonephritis	Crescentic glomerulonephritis	Patchy cortical necrosis
Duration of transplant (years)	5	4	3
Preconceptional creatinine (mg/dl)	1	1.8	1.5
Immunosuppressive agents	Tab prednisolone + azathioprine	Tab prednisolone	Tab prednisolone + azathioprine + tacrolimus
Associated medical condition	None	Hypertension since 4 years	Hypothyroidism + hypertension since 2.5 years
Treatment for infertility taken so far	2 cycles of IVF—failed	3 cycle of IVF—failed	IVF—donor oocyte

^a Associated with PID

There was positive history of gestational hypertension in previous pregnancy in 9 patients, which led to acute renal failure in 2 patients and chronic renal failure in 7 patients, necessitating renal transplant for survival. The reason for renal transplant might be inappropriate control of blood pressure or poor compliance in taking antihypertensive drugs in postpartum period, which might have led to renal failure.

The mean preconceptional serum creatinine was 1.15 ± 0.31 mg/dl. Fertility outcome with respect to their preconceptional serum creatinine was studied (Table 1), where out of 3 infertile patients, 2 patients had serum creatinine levels >1.2 mg/dl.

The main cause of infertility in these patients was ovarian factor (in 2 patients) and tubal factor in 1 patient. Among 16 patients, 8 patients had missed abortion, 2 patients had preterm deliveries and 6 patients had term deliveries.

Infertility in renal transplant recipient was studied (Table 2). One patient had premature ovarian failure, one had bilateral tubal block, and one had low ovarian reserve. All of these patients were infertile before transplant, and

the cause of infertility may be due to underlying renal pathology.

Discussion

Female patients with chronic kidney disease or with end-stage renal disease can be presented with sexual dysfunction and infertility before transplant. Sexual dysfunction can be in the form of decreased libido, difficulty in achieving orgasm, lack of vaginal lubrication and dyspareunia. The reason for infertility is due to disturbed pulsatile secretion of GnRH, which may be associated with high follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin levels [1]. These hormonal disturbances can reverse after transplant, resulting in normal ovulatory cycles and regular menstruation [4, 5]. However, female patients with chronic kidney disease may develop early menopause, 4.5 years earlier than general population [6]. One of our infertile patients also had premature ovarian failure, who was advised for in vitro fertilization with donor oocyte.

Peritransplant period and counseling play a vital role in predicting fertility outcome in renal transplant recipients. These patients need to be counseled about appropriate time to conceive while keeping in mind about risk of premature menopause which might be due to preexisting renal pathology. Initially, 2 years following successful transplantation was considered to be the best time to conceive. It has been replaced by the American Society of Transplantation Consensus Opinion that as long as graft function is good, patient can conceive. Graft function is considered to be optimum when serum creatinine was <1.5 mg/dl, with <500 mg/24-h protein excretion [7]. Many of these patients restore their fertility following 1–12 months after renal transplant [8]. However, recovery of fertility is less common in women undergoing transplant who are close to the end of their childbearing age.

These patients can have ovulatory cycles within 1–2 months of transplantation; hence, they also require appropriate contraceptive counseling immediately after transplantation. Low-dose estrogen–progesterone oral contraceptive preparation is preferred over intrauterine devices [9], because these patients are already on immunosuppressive drugs, thereby increasing risk of infection with use of intrauterine devices.

The most commonly used immunosuppressive agents are corticosteroids, azathioprine, cyclosporine, tacrolimus, sirolimus and mycophenolate mofetil. Out of these drugs, sirolimus is associated with male and female infertility and tacrolimus is associated with asthenoteratospermia if dose was >2 mg/kg/day. In male, sirolimus causes testicular atrophy with significantly reduced total sperm count, whereas in female, it causes amenorrhea and menstrual irregularity [10]. It is recommended that whenever patient is planning to conceive, sirolimus should be replaced by cyclosporine.

The above-mentioned immunosuppressive agents can have effect on fetal organogenesis and growth during pregnancy. The current recommendations are to avoid mycophenolate mofetil and rapamycin for 6 weeks before pregnancy because they are associated with severe structural deformities [7, 11]. Tacrolimus and cyclosporine are included in FDA category C, while steroids are included in FDA category B.

The pregnancy rate in renal transplant recipients in childbearing age is 5–12 % [12]; in our study, pregnancy rate was 7.35 %. There are reports on infertile renal transplant recipients who had undergone successful in vitro fertilization treatments [13–15]. Pregnancy in renal transplant recipient is a high-risk pregnancy, which can get more complicated with in vitro fertilization treatment due to the risk of multiple births [16]. Pregnancy in renal transplant recipients is associated with increased risk of graft rejection leading to renal damage

and also at risk of developing gestational hypertension, preeclampsia, infections, preterm deliveries and premature rupture of membranes. But with close monitoring during antenatal and postpartum period, these complications can be managed.

Conclusion

Renal transplant recipients are high-risk patients who require special care and counseling starting from peritransplant and preconceptional period to their postpartum period. These patients can have good fertility as well as good pregnancy outcome following optimization of graft function.

Compliance with Ethical Standards

Conflict of interest None.

Ethical Approval It is an observational study carried out at IKDRC, Ahmedabad. The study does not involve experiment on any animal or human being.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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