

# Successful pregnancy following single blastocyst transfer in a renal transplant recipient

V. Arun Muthuvel,  
Manipriya Ravindran,  
Aravind Chander<sup>1</sup>,  
Chandralekha Veluswamy

Department of Reproductive Medicine, Iswarya Women's Hospital and Fertility Centre, Chennai, <sup>1</sup>Department of Reproductive Medicine, Iswarya Women's Hospital and Fertility Centre, Coimbatore, Tamil Nadu, India

**Address for correspondence:**

Dr. V. Arun Muthuvel,  
Department of Reproductive Medicine, 1<sup>st</sup> Main Road, Kasturba Nagar, Adyar, Chennai - 600 020, Tamil Nadu, India.  
E-mail: arunmuthuvel@gmail.com

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## ABSTRACT

Numerous spontaneous pregnancies have been reported in renal transplant recipients; however, only a few pregnancies after the use of assisted reproductive techniques. The authors report a case of renal transplant recipient with secondary infertility who delivered a healthy baby without any complications. The report highlights the importance of minimal stimulation protocol during ovarian stimulation, single embryo transfer, and the need for multispecialty care for these patients. To the best of the authors' knowledge, the present report is the first such case from India and also the second in the world to report a blastocyst transfer among renal transplant recipients.

**KEY WORDS:** *In vitro* fertilization, infertility, renal transplant, single embryo blastocyst transfer

## INTRODUCTION

Clinical management of infertility among organ transplant recipients is a challenge to the treating physician with hitherto limited information in literature. In particular, artificial reproductive techniques (ART) have been seldom attempted among these patients due to the possibility of life-threatening complications. The tremendous progress in the fields of ART and transplantation medicine offers the opportunity to safely explore various options for pregnancy. The authors present a case of a young postrenal transplant female with secondary infertility who successfully delivered a healthy baby following a single blastocyst transfer.

Other clinical and biochemical parameters were found to be normal. Ultrasound with Doppler revealed normal transplant kidney with mild polycystic ovary disease. The patient's basal hormone profile worked on day three of menstrual cycle as follows: Luteinizing hormone (LH) - 8.28 mIU/mL, follicle-stimulating hormone (FSH) - 4.04 mIU/mL, prolactin - 19.03 ng/mL, and anti-mullerian hormone - 4.1 ng/mL. Antral follicular count was more than 24 follicles indicative of polycystic ovarian morphology. Semen analysis of the patient's husband was normal. Hence, intra-uterine insemination was tried for four cycles. All the cycles were ovulatory with appropriate endometrial lining. However, she failed to conceive.

## CASE REPORT

A 30-year-old woman, married for 8 years was referred with a desire to conceive. At the age of 23, she conceived spontaneously but suffered a miscarriage. Following this pregnancy, she failed to conceive naturally. She underwent renal transplant for immunoglobulin A nephropathy at the age of 26. At the time of presentation to the authors, she was on tacrolimus, azathioprine, and prednisolone. Her serum blood urea nitrogen and creatinine were within normal limits (14 mg/dl and 0.8 mg/dl, respectively).

The option of *in vitro* fertilization (IVF) was opted by the couple after being fully counseled of the potential risks associated

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with ART and pregnancy. Following a discussion with the nephrologists and high-risk pregnancy specialist, IVF cycle was planned and initiated without precycle suppression with oral contraceptive pills. A mild stimulation protocol with recombinant FSH 150 IU/day (injection Gonal F, Merck KGaA) was started on day 3 and continued for 5 days. Follicular monitoring was started on day 6. Dose adjustment was done on day 8. Recombinant FSH dose was reduced to 75 IU/day and continued till day 11. Gonadotropin-releasing hormone (GnRH) antagonist, injection Cetrotex acetate 250 mcg (injection Cetrotide, Merck KGaA) was administered subcutaneously on menstrual cycle day 7 and continued until ovulation trigger. She developed 12 follicles, each more than 16 mm in size. Ovulation was induced with injection Triptorelin 0.2 mg (injection Decapeptyl 0.2 mg, Ferring pharmaceuticals), when more than 3 follicles measured >17 mm. After 35 h, oocyte retrieval was done under ultrasound guidance with intravenous sedation. Injection human chorionic gonadotropin (HCG) 1500U was administered immediately after oocyte retrieval to rescue the luteal phase. Then, 10 mature oocytes were retrieved and all the 10 oocytes were subjected to ICSI. On day 3, eight excellent quality embryos developed and extended culture was done till day 5. Endometrial thickness was 8 mm and a single expanded blastocyst was transferred with Labotect catheter. Seven other good quality blastocysts were cryopreserved.

Luteal phase support was started 24 h after oocyte retrieval and continued until 8 weeks with 90 mg progesterone gel (Crinone 8% gel, Merck KGaA) once a day. The patient did not develop any signs or symptoms of ovarian hyperstimulation syndrome (OHSS). Serum beta HCG levels were estimated to be 800 IU on day 14 of embryo transfer. Transvaginal ultrasound was performed 2 weeks after embryo transfer and single viable fetus corresponding to 6 weeks was observed. Throughout the treatment cycle and during pregnancy, the patient's anti-rejection drugs (prednisolone, tacrolimus, and azathioprine) were continued at maintenance doses.

The patient was monitored vigilantly and the entire course of pregnancy was uneventful with normal blood pressure and renal function. There was no proteinuria observed during weekly urine monitoring and the patient did not develop any signs of preeclampsia. In addition, growth of the fetus was monitored at regular intervals. Cesarean section was performed electively at 37 weeks and the patient delivered a healthy male baby weighing 3.2 kg. There was no evidence of graft rejection thereafter.

## DISCUSSION

In 1995, the first successful IVF in a renal transplant recipient was performed by Lockwood *et al.*<sup>[1]</sup> The first successful blastocyst transfer in a renal transplant recipient was reported in 2008 by Fichez *et al.*<sup>[2]</sup> To the best of the authors' knowledge, there have been only 7 cases reported till the year 2015, on successful pregnancies after IVF in renal transplant recipients. Renal insufficiency disrupts the normal gonadal function due to dysfunction of hypothalamo-pituitary-gonadal axis resulting in high FSH, LH, and prolactin levels.<sup>[3]</sup> This hormonal pattern results in infertility.<sup>[4]</sup> After successful transplantation, subsequent spontaneous pregnancies have been reported in 12% of the women in reproductive age. Many studies have claimed that the fertility is restored in 1 to 3 years following transplantation.<sup>[5]</sup> The risk of graft rejection is high during the 1<sup>st</sup> year and therefore it is not advised to plan IVF within that period.

This was the only case to have safely delivered a 37 weeks term baby without any maternal and neonatal complications. Maternal complications during pregnancy are pregnancy-induced hypertension, preeclampsia, deep vein thrombosis, infections, and graft rejection while the fetal complications include preterm birth, very low birth weight, intrauterine growth restriction, or small for gestational age babies.<sup>[6]</sup> OHSS is one the complications that can arise during ovulation induction. This can be attributed to the altered metabolism of the recombinant FSH which in turn is due to the impaired renal function. Further, enlarged ovaries can rarely obstruct the transplanted kidney during induction resulting in deterioration of renal function.<sup>[7]</sup>

The present case report did not develop OHSS despite having polycystic ovaries because of the mild stimulation protocol with vigilant monitoring. Step down protocol with reduction in gonadotropin dosage was used. The risk of OHSS was reduced to a significant extent by triggering final oocyte maturation with GnRH agonist trigger and using small dose of HCG after oocyte retrieval. Single embryo transfer is recommended while the remaining embryos could be cryopreserved to avoid complications that arise from multiple pregnancies.

It is also recommended that transplant recipients satisfy certain criteria before contemplating pregnancy to avoid complications [Figure 1]. Although pregnancy causes an increase in glomerular filtration rate, hyperfiltration is compensated by the normal intraglomerular pressure. Therefore, no glomerular damage occurs if allograft function is normal prior to pregnancy.<sup>[8]</sup> According to Alston *et al.*, the graft rejection rate among posttransplant

- 1-3years post renal transplantation
- Normal allograft ultrasound and doppler
- Stable graft function
- No graft rejection in the last year
- Normal renal function - Serum creatinine <2mg/dl
- BP= 140/ 90 mm Hg with medications
- Proteinuria < 500 mg/day
- On maintenance dose of immunosuppressive agents as advised by the transplant physician
- To alternate teratogenic drugs taken by the patient

**Figure 1:** Criteria to consider pregnancy among renal transplant recipients

pregnancies is 6%, which is similar to that of a nonpregnant population.<sup>[9]</sup> With more such successful cases, the number of transplant recipients seeking assisted reproduction is likely to increase.

## CONCLUSION

With increasing cases of renal transplantation, women approaching for infertility treatment are expected to increase and more complicated cases have to be dealt with. It is safe to plan pregnancy through ART for renal transplant recipients under vigilant multi-specialty care. It is prudent to initiate mild stimulation protocol and trigger final oocyte maturation with a GnRH agonist to avoid complications such as OHSS. Single embryo transfer is recommended to avoid the complications of multiple pregnancies.

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## Conflicts of interest

There are no conflicts of interest.

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