

Pregnancy outcomes in renal transplant recipients

INTRODUCTION

Renal transplantation improves reproductive function in a patient with end-stage renal disease.^[1] Due to altered physiology and immunosuppressant therapy, renal recipients have a higher risk of both maternal and foetal complications than a healthy normal parturient.^[2] The incidence of gestational diabetes, pre-eclampsia, preterm delivery, foetal growth restriction and caesarean section is higher in renal recipients than in general. A multidisciplinary team consisting of obstetricians, nephrologists, neonatologists and anaesthesiologist should be involved early for the safe management of these patients. Multiple studies have reported successful obstetric and neonatal outcomes in renal recipients.^[3] We retrospectively reviewed the pregnancy outcomes of 20 patients who had undergone renal transplantation and presented to a tertiary care hospital for safe confinement during the period 2011–2017.

METHODS

This was a retrospective study, where we reviewed the obstetric case records of 20 renal transplant recipients who presented for safe confinement in our institute from 2011 to 2017. After obtaining institutional ethics committee clearance (IEC-AIMS-2018-ANES-054), clinical and management details were obtained from the hospital records. The demographic and obstetric details, indication for renal transplantation, transplantation-pregnancy interval, maternal comorbidities, mode of delivery, anaesthetic management, pre and post-delivery renal function and foetal outcomes were analysed.

RESULTS

Among the 20 patients, eighteen had undergone renal transplantation in our institute and two were from an outside centre. All patients had received live related donor renal transplants. The mean age of the parturients was 28.1 years, the mean transplantation-delivery interval was 6.3 years [Table 1]. They were on immunosuppressants, which were continued in the perioperative period. Strict aseptic precautions and prophylactic antibiotics were used to avoid infection,

which included a single dose of intravenous (IV) cefuroxime 1.5 gm for caesarean delivery and amoxicillin-clavulanate 1.2 gm for normal vaginal delivery. Eighty-five per cent (17/20) of patients were primigravidas with a singleton pregnancy. The mean gestational age at delivery was 36.2 weeks. Seventy percent of patients (14/20) had chronic hypertension and 30% (6/20) had diabetes mellitus. Seventy-eight percent (14/18) of caesarean sections were performed under subarachnoid block and 22% (4/18) under epidural anaesthesia. Ninety percent (18/20) underwent caesarean section, of which 50% (9/20) were taken on an emergency basis. Ten percent (2/20) underwent full-term normal vaginal delivery under epidural analgesia [Table 2]. Hypotension following spinal anaesthesia was managed with IV phenylephrine boluses. Patients were monitored with five lead electrocardiogram, saturation probe and non-invasive blood pressure. Invasive lines were not used. Three patients received leukodepleted packed red cell units intraoperatively. No significant maternal anaesthetic complications were encountered in the intraoperative and postoperative periods. Epidural analgesia was continued in the postoperative period with 0.1% ropivacaine. Patients not having epidural catheter were given bilateral transversus abdominis plane block with 30ml of 0.1% ropivacaine after surgery. Patients were monitored in the postoperative recovery for 6 hours and no patient required transfer to the intensive care unit (ICU).

In our series, six patients had high preoperative creatinine levels (>1.5mg/dl), which improved when pregnancy was terminated. One of the patients was taken up for caesarean section at 30 weeks in view of deteriorating renal function. Others had stable renal function and normal serum potassium levels [Table 3]. We did not encounter graft rejection in any of our patients. One of the parturients who developed placental abruption underwent emergency caesarean section under spinal anaesthesia and the baby was shifted to neonatal ICU and ventilated due to birth asphyxia. Six babies were delivered preterm and four of them required neonatal ICU care. The mean birth weight was 2.63kg.

DISCUSSION

According to the American Society of Transplantation consensus opinion, pregnancy can be planned after a year if graft function is optimal with a stable dose of immunosuppressants and

Table 1: Indication for transplant and transplant pregnancy interval

Patient No	Age at pregnancy (years)	Indication of Renal Transplant	Transplant pregnancy interval (years)
1	27	Chronic glomerulonephritis	8
2	29	Chronic glomerulonephritis	7
3	26	Chronic tubule-interstitial disease	11
4	24	Native renal disease not known	6
5	31	Focal segmental glomerulosclerosis	5
6	25	Membranoproliferative Glomerulonephritis	3
7	38	Unknown native disease	5
8	25	Crescentic glomerulonephritis	3
9	29	Chronic interstitial nephritis	8
10	23	Chronic tubulointerstitial nephritis	5
11	27	Primary glomerular disease	7
12	29	Polycystic kidney disease	6
13	27	Chronic interstitial nephritis	8
14	23	Membranoproliferative Glomerulonephritis	5
15	33	Lupus nephritis	2
16	32	Membranoproliferative Glomerulonephritis	7
17	27	Membranoproliferative Glomerulonephritis	13
18	28	Membranoproliferative glomerulonephritis	10
19	29	Glomerular sclerosis and Interstitial fibrosis	3
20	30	Lupus glomerulonephritis	4

Table 2: Maternal data, type of delivery and anaesthesia

Patient No	Gravida/Parity	Gestational Age (weeks)	Maternal comorbidities	Type of Delivery	Type of Anaesthesia
1	G2/P1/A1	36	Preeclampsia	LSCS (Emergency)	SAB
2	G1/P1	37	Chronic hypertension	LSCS (Elective)	SAB
3	G1/P1	34	Gestational diabetes, Chronic hypertension	LSCS (Elective)	SAB
4	G1/P1	37	Gestational diabetes, Chronic hypertension	LSCS (Elective)	SAB
5	G1/P1	37	Chronic hypertension with superimposed pre-eclampsia	FTND	EA
6	G1/P1	37	Chronic hypertension Abruptio placenta grade 2	LSCS (Emergency)	SAB
7	G1/P1	37	Overt diabetes	FTND	EA
8	G1/P1	35	Chronic hypertension with superimposed pre-eclampsia	LSCS (Emergency)	SAB
9	G1/P1	30	Chronic hypertension	LSCS (Emergency)	SAB
10	G1/P1	35	Overt diabetes	LSCS (Elective)	SAB
11	G1/P1	37	Chronic hypertension	LSCS (Elective)	SAB
12	G1/P1	37	Chronic hypertension	LSCS (Elective)	SAB
13	G1/P1	37	Chronic hypertension	LSCS (Elective)	SAB
14	G1/P1	38	Cholestasis of pregnancy	LSCS (Emergency)	EA
15	G3/P1/A2	37	Chronic hypertension with superimposed pre-eclampsia	LSCS (Emergency)	SAB
16	G2/P1/A1	38	Chronic hypertension	LSCS (Emergency)	EA
17	G1/P1	37	Gestational diabetes	LSCS (Emergency)	EA
18	G1/P1	37	Chronic hypertension	LSCS (Emergency)	SAB
19	G1/P1	37	Gestational diabetes	LSCS (Elective)	EA
20	G1/P1	34	Chronic hypertension	LSCS (Elective)	SAB

SAB: Sub-arachnoid block, EA: Epidural analgesia, LSCS: Lower segment caesarean section, FTND: Full term normal delivery

not on any teratogenic medications.^[4-6] The graft function is considered optimal if serum creatinine is <1.5 mg/dl with <500 mg/24 h protein excretion. Hypertension is common in these patients prior to conception. A high incidence of hypertension is attributed to chronic use of corticosteroids and increased production of renin by the native kidney. It is difficult to diagnose superimposed preeclampsia due to the presence of pre-existing hypertension

and proteinuria.^[7]A marked increase in proteinuria with sudden worsening of hypertension may also be a sign of acute graft rejection. High-dose steroids are used to treat acute rejection during pregnancy. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are discontinued before pregnancy.^[6] Blood pressure higher than 140/90 mmHg is treated with beta-blockers, hydralazine, thiazide diuretics or labetalol.^[8,9]

Table 3: Laboratory values pre and post caesarean section

Patient number	Se creatinine		Blood urea		Se potassium	
	Pre	Post	Pre	Post	Pre	Post
	LSCS	LSCS	LSCS	LSCS	LSCS	LSCS
1	1.59	1.43	21	40.3	3.8	4.4
2	1.06	1.1	26.1	29.7	5.3	3.9
3	0.9	1.21	24.9	26.2	3.5	3.6
4	1.28	1.3	25.6	31.2	4.1	3.9
5	1.3	1.4	28.2	31.4	4.3	3.4
6	1.1	1.2	25.3	51.3	5.0	4.5
7	1.61	1.60	29.4	53.6	4.7	4.2
8	1.5	1.1	34.4	31.2	4.2	3.9
9	3.2	2.7	21.6	64.1	4.3	3.9
10	1.49	1.48	33.7	33.2	3.1	3.8
11	1.05	1.13	34.1	16.3	4.8	4.2
12	1.27	1.31	27.2	31.3	4.1	3.3
13	1.36	1.33	25.7	28.2	4.3	3.9
14	1.33	1.56	31.8	35.8	4.0	3.7
15	0.70	0.83	23.2	15.1	3.7	3.7
16	1.0	1.0	23.5	22.8	3.8	3.6
17	1.88	1.69	25.1	30.0	3.9	3.7
18	0.66	0.65	10.5	9.8	4.3	4.1
19	1.32	1.39	28.1	42.5	4.7	3.7
20	1.32	1.37	27.9	31.2	4.6	3.9

Se - Serum; LSCS - Lower segment caesarean section; Values of Se Creatinine are in mg/dL, Blood urea level in mg/dL, Se Potassium in mmol/L

Renal recipients are prescribed immunosuppressants to prevent rejection. The immunosuppressive drugs commonly used are mycophenolate mofetil, calcineurin inhibitors including tacrolimus and cyclosporine, azathioprine and steroids. Mycophenolate mofetil can cause MMF foetal syndrome and is contraindicated in pregnancy.^[9] It has to be discontinued and switched to azathioprine 6 week before planning for pregnancy. It causes first-trimester pregnancy loss and congenital malformations.^[8] Cyclosporine causes hypertension, hyperlipidaemia, nephrotoxicity, neurotoxicity and hepatotoxicity. Requirement of cyclosporine and tacrolimus increases by 25% during pregnancy due to the increase in the volume of distribution and cytochrome P450 activity. Cyclosporine trough levels decrease by an average of 23% in the first trimester, 39% in the second trimester and 29% in the third trimester. Hence, frequent monitoring of the whole blood trough level twice weekly in the first and second trimesters, weekly in the third trimester and a week after delivery is recommended.^[8] Before pregnancy, tacrolimus is titrated to a trough concentration of 5–10ng/ml to prevent graft rejection. Tacrolimus levels are checked monthly during pregnancy.

Anaesthetists are involved in providing labour analgesia and anaesthesia. The anaesthetic plan depends on the functional status of the transplanted

kidney and the indication for caesarean section. Studies have shown that both general and regional anaesthesia can be safely used. If coagulation status is normal, the regional anaesthetic technique is preferred over general anaesthesia. The concerns are the interaction of immunosuppressants with anaesthetic medications. Cyclosporine can cause tremors, seizures, and paraesthesia. Its documentation is important before performing a regional anaesthetic. Immunosuppressants can cause a rise in liver enzymes. Azathioprine and mycophenolate can cause bone marrow suppression. Glucocorticoids cause sodium retention, hypertension, diabetes, osteoporosis, poor skin integrity and peptic ulcer disease. Hence, preoperative assessment of patients should include laboratory investigations such as complete blood count, electrolytes, blood glucose renal and liver function tests. Immunosuppressants are continued to maintain the therapeutic level of the drug. Tacrolimus is administered 4–7 hours before surgery as it delays gastric emptying [Table 4]. The drugs that have an effect on cytochrome P-450 3A metabolism like cimetidine, omeprazole, fluconazole, voriconazole, metoclopramide, diltiazem, nicardipine and verapamil may alter the immunosuppressant drug levels and are avoided. Ampicillin and amoxicillin are the first-choice antibiotics in patients with renal disease. Clavulanic acid and cephalosporins are also used.

A stress dose of steroids is given prior to surgery to avoid refractory hypotension. Aspiration prophylaxis with ranitidine and careful handling of skin and bones are required. Meticulous peri-operative fluid management is followed to avoid hypotension and urine output of more than 1 ml/kg/h is maintained. There is no clear recommendation on preloading or coloadng in renal transplant recipients coming for caesarean section. However, it is better to avoid preloading in an already compromised renal patient. Spinal induced hypotension is aggressively managed with coloadng and intravenous phenylephrine to maintain sufficient renal perfusion. Due to previous abdominal surgery, prolonged surgical time should be anticipated. To achieve adequate level of block of T4, we used our standard institutional protocol of 9–11mg of hyperbaric 0.5% bupivacaine with 10µg fentanyl. Renal impairment is not a contraindication for the use of oxytocin or prostaglandins. Ergometrine is avoided in patients with hypertension.

Renal recipients may have normal creatinine levels but their glomerular filtration rate and effective

Table 4: Immunosuppressant medication

Commonly used immunosuppressants	Dose modification	Advice on continuation
Mycophenolate mofetil	-	Discontinue 3 months before pregnancy
Cyclosporine	20-25% dose elevation	Continue
Tacrolimus	20-25% dose elevation	Dose administered 4-7 h before surgery
Azathioprine	≤2 mg/kg	Continue
Steroids	Prednisone ≤15 mg/day	Continue

plasma flow may be low. Hence, if general anaesthesia is required, prolonged action of drugs should be anticipated. In pregnancy, rapid sequence induction with thiopentone is preferred. Succinyl choline can be used if there is no preoperative hyperkalemia. Among inhalational agents, sevoflurane is considered safe and enflurane is avoided. Cyclosporine prolongs action of thiopentone, fentanyl and neuromuscular blocking agents. The neuromuscular function is monitored and atracurium or cisatracurium, which do not depend on renal excretion are preferred as muscle relaxants. Postoperative pain relief is provided with transversus abdominis plane block, epidural or parenteral opioids. Non-steroidal anti-inflammatory drugs are avoided as they can worsen renal function and exacerbate cyclosporine toxicity. Epidural catheters are removed within 48 hours to avoid epidural abscess.

Vaginal delivery is preferred in renal recipients and caesarean sections are performed only for obstetric indications. The transplanted kidney in the pelvis is unlikely to be injured during vaginal delivery. The use of instrumental delivery is minimised. During renal transplantation, the graft is placed extraperitoneal, mostly in the right iliac fossa. It lies close to the lower uterine segment. The muscles of the anterior abdominal wall may be adherent to the transplanted kidney. Proper planning by ultrasound or magnetic resonance imaging is advisable to identify the location of the graft. A vertical midline incision is used to avoid injury to the transplanted kidney by direct or shearing forces. It is a protocol in our institute that a member of the transplant team (urologist) has to assist the operating obstetrician during caesarean section. Following delivery, antihypertensives and immunosuppressants are restarted. Patients on tacrolimus have to avoid breastfeeding up to 4 hours after taking a dose.^[10] Patients on cyclosporine are advised against breastfeeding.

CONCLUSIONS

Despite the apprehension among renal recipients, our experience suggests that planned pregnancies

have a good obstetric and neonatal outcome. A multidisciplinary team consisting of obstetricians, nephrologists, neonatologists and anaesthesiologists are required to manage these patients. These patients can safely undergo lower segment caesarean section under regional anaesthesia or have labour epidural analgesia for normal vaginal delivery with minimal side effects.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

**Nitu Puthenveetil, Anish Mohan, Sajan Rahman,
Jerry Paul**

Department of Anaesthesiology and Critical Care, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi, Kerala, India

Address for correspondence:

Dr. Nitu Puthenveetil
Department of Anaesthesia and Critical Care, Amrita
Institute of Medical Sciences, Kochi - 682 041, Kerala, India.
E-mail: nituveesundeeep@gmail.com

Submitted: 26-Apr-2021

Accepted: 14-Sep-2021


Published: 08-Oct-2021

REFERENCES

- Deshpande NA, James NT, Kucirka LM, Boyarsky BJ, Garonzik-Wang JM, Montgomery RA, et al. Pregnancy outcomes in kidney transplant recipients: A systematic review and meta-analysis. *Am J Transplant* 2011; 11:2388-404.
- Shah S, Venkatesan RL, Gupta A, Sanghavi MK, Welge J, Johansen R, et al. Pregnancy outcomes in women with kidney transplant: Metaanalysis and systematic review. *BMC Nephrology* 2019; 20:24.
- Warzecha D, Szymusik I, Grzechocinska B, Cyganek A, Kociszewska-Najman B, Mazanowska N, et al. *In vitro* fertilization and pregnancy outcomes among patients after kidney transplantation: Case series and single-center experience. *TransplantProc* 2018;50:1892-5.
- Piccoli GB, Cabiddu G, Attini R, Gerbino M, Todeschini P, Perrino ML, et al. Outcomes of pregnancies after kidney transplantation: Lessons learned from CKD. A comparison of transplanted, nontransplanted chronic kidney disease patients and low-risk pregnancies: A multicenter nationwide analysis. *Transplantation* 2017; 101:2536-44.
- Baker RJ, Mark PB, Patel RK, Stevens KK, Palmer N. Renal association clinical practice guideline in post-operative care in the kidney transplant recipient. *BMC Nephrology*

- 2017;18:174.
6. Josephson MA, McKay DB. Women and transplantation: Fertility, sexuality, pregnancy, contraception. *Adv Chronic Kidney Dis* 2013;20:433-40.
 7. Zachariaha MS, Tornatorea KM, Venuto RC. Kidney transplantation and pregnancy. *Curr Opin Organ Transplant* 2009;14:386-91.
 8. Cabiddu G, Castellino S, Gernone G, Santoro D, Moroni G, Giannattasio M, *et al.* A best practice position statement on pregnancy in chronic kidney disease: The Italian Study Group on kidney and pregnancy. *J Nephrol* 2016; 29:277-303.
 9. Upadya M, Rao ST. Hypertensive disorders in pregnancy. *Indian J Anaesth* 2018; 62:675-81.
 10. Goyal VK, Solanki SL, Baj B. Pulmonary hypertension and postoperative outcome in renal transplant: A retrospective analysis of 170 patients. *Indian J Anaesth* 2018; 62:131-5.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online	
Quick response code	Website: www.ijaweb.org
	DOI: 10.4103/ija.ija_362_21

How to cite this article: Puthenveetil N, Mohan A, Rahman S, Paul J. Pregnancy outcomes in renal transplant recipients. *Indian J Anaesth* 2021;65:695-9.