


Pregnancy after kidney and liver transplantation

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Pregnancy in kidney and liver transplant recipients presents unique challenges and risks for both maternal and fetal health. This article examines the management of pregnancy in kidney and liver transplant recipients, focusing on pre-pregnancy counselling, trimester-specific care, the teratogenic effects of immunosuppressive drugs, and the role of the multidisciplinary team. While South African (SA) data on this topic are limited, the Transplant Pregnancy Registry International has provided valuable insights. Despite the increased risk of maternal and fetal complications, the overall risk of graft loss during pregnancy is low. Graft survival rates are comparable between pregnant and non-pregnant transplant recipients, except for pregnancies occurring within 1 year of transplantation. By addressing the complexities of managing pregnant women with kidney or liver transplants, this article underscores the importance of tailored care and the involvement of various medical specialists. It also explores the safety of and potential complications associated with specific immunosuppressive therapies during pregnancy. Further research is needed to enhance our understanding and optimise the management of these high-risk pregnancies in SA.

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The first successful solid-organ transplant was performed in 1954, when Joseph Murray transplanted a kidney into a patient from the patient's twin brother.^[1] The first pregnancy in a transplant recipient occurred 3 years later, in 1957, when a 21-year-old woman who had received a kidney transplant from her twin sister in 1956 became pregnant. She delivered a healthy male infant in 1958.^[2] The first liver transplant was performed in 1967, which was followed by the first pregnancy in a liver transplant recipient in 1978.^[3]

As of December 2020, the Transplant Pregnancy Registry International (TPRI) had reported 3 433 pregnancies in 1 909 women since its inception in 1991. These included 1 279 women with kidney transplants (2 270 pregnancies) and 366 with liver transplants (724 pregnancies).^[4] Interestingly, in the USA, the live birth rate in women who have had liver and kidney transplants is higher than that in the general population. However, adverse outcomes such as pre-eclampsia and preterm delivery are more common in transplant recipients.^[5,6]

While the Organ Donor Foundation reports numbers of transplants performed per year in South Africa (SA), data on pregnancy after organ transplantation in SA are limited. A literature search revealed three reports – the first from 1976,^[7] reporting on 10 women (out of 48 female renal transplant recipients) with 15 pregnancies, the second from 1985,^[8] examining outcomes in 38 pregnancies in 21 renal transplant recipients, and the third in 2011,^[9] that reviewed five pregnancies in four liver transplant recipients. Since 2016 there have been six pregnancies from SA reported to the TPRI, although it is unclear what organ was transplanted in these cases.^[4] Despite the small numbers reported in the SA literature, it is important for all involved in the care of women and female children with chronic kidney or liver disease to be aware of the reproductive issues of women pre- and post-kidney or liver transplant.

Kidneys and livers are the most commonly transplanted organs in SA, accounting for 68% and 17%, respectively of the 3 660 solid-

organ transplants performed between 2009 and 2019.^[10] While national data on the gender and age of transplant recipients are not available, a report published by Discovery Health Medical Scheme, which funded 26% of all transplants in SA between 2009 and 2021, including 31.4% of all kidney and 49.7% of all liver transplants, gives valuable insight into transplants in SA.^[11] The median age at transplant was 43 and 47 years for kidney and liver transplants, respectively, and 39% of kidney and 44% of liver transplant recipients were female.^[11]

This review focuses on the considerations from preconception to post-delivery in women following kidney and liver transplantation. We highlight the importance of evaluation by a multidisciplinary team (MDT), including maternal-fetal medicine specialists, obstetricians, obstetric physicians, transplant physicians and transplant surgeons, to ensure the best possible outcomes for both mother and baby.

Fertility issues

Chronic illness is known to have a negative impact on female fertility, including in women with end-stage kidney or liver disease. Many of these women experience amenorrhoea or irregular menstrual cycles, often without ovulation.^[12-14] Transplantation can improve fertility, restoring regular menses and ovulatory cycles as early as 3 weeks post-transplant.^[15-17] Eighty percent of women report normal menstruation returning within the first year post-transplant, with this being less likely in women who undergo transplantation near the end of their reproductive years.^[12,18] For these individuals and those in whom pregnancy after a transplant is considered too high risk, alternative options such as oocyte cryopreservation prior to transplantation, surrogacy or adoption should be explored.

While prepubertal girls do not face immediate fertility concerns, it is crucial to provide counselling to their caregivers on the importance of reproductive health, contraception, and future pregnancy planning. As females enter puberty, age-appropriate discussions, and opportunities to engage with healthcare providers, must be provided to ensure that they have access to the appropriate information and resources for their reproductive health. Most centres lack a formal transition programme from paediatric to adult care at the time of puberty, which may make these discussions particularly difficult.^[19,20] Adolescent female patients may be faced with a new and unfamiliar healthcare team and a system less equipped to manage the complex care of adolescent patients (aged 10 - 19 years).^[21]

Adolescence is a high-risk period for graft rejection; one SA study demonstrated a graft failure rate of 74.5% in adolescent renal transplant patients, although the majority (62.2%) occurred in male patients.^[22] Non-compliance is also of major concern in adolescent patients, who have a high risk of unplanned pregnancy^[23] and therefore need to be on and adherent to contraception. This issue is particularly relevant in SA, where 13.4% of all births registered in 2022 occurred in women aged 10 - 19 years^[24] and teenage pregnancies increased by 48.7% between 2017 and 2021 across the country.^[25] The lack of adolescent medicine as a subspecialty in SA adds to the difficulty patients may experience when transitioning from paediatric to adult care.^[21]

Contraceptive options

In kidney and liver transplant recipients of reproductive age, a contraceptive plan should be established prior to the transplant, with consideration given to the type and timing of contraception. The choice of contraception is largely influenced by the recipient's comorbidities, as well as their current immunosuppressive drug therapy. For instance, mycophenolate-containing drugs may decrease the efficacy of certain combined oral contraceptives

by reducing the systemic exposure to levonorgestrel, while not affecting the systemic exposure to ethinyloestradiol.^[26] The SA national contraceptive clinical guidelines^[27] and the World Health Organization's medical eligibility criteria for contraceptive use^[28] do not explicitly discuss transplant recipients, but the US medical eligibility criteria for contraceptive use, issued by the Centers for Disease Control in 2016 and updated in 2020, does.^[29] They divide women with solid-organ transplants into those with 'stable uncomplicated graft function', for whom all methods of contraception are considered safe, and those with 'complicated graft function', in whom oestrogen should be avoided. Various contraceptive methods are reviewed in Table 1.

Preconception counselling

While prenatal care is offered for free at all primary healthcare clinics, these services are underutilised in both sub-Saharan Africa and SA.^[32,33] Transplant recipients should be counselled on factors associated with good pregnancy outcomes. These include delaying pregnancy for at least 1 year following the transplant, no evidence of graft rejection for at least 1 year prior to conception, stable graft function, absence of acute infections, stable maintenance doses of immunosuppressant drugs, and normal blood pressure.^[30,34]

It is of crucial importance for women who wish to conceive to be counselled on the potential teratogenicity of immunosuppressive drugs. Mycophenolate-containing drugs are teratogenic and should be discontinued at least 6 weeks prior to stopping contraception.^[35] Prolonged high-dose corticosteroids may increase the risk of intrauterine growth restriction (IUGR) and low birthweight.^[36] Azathioprine has established safety data in human pregnancies and is a safe option.^[37] Alternative options for use during pregnancy include cyclosporine^[38] and tacrolimus.^[39] A full summary of immunosuppressive drugs and their use in pregnancy is provided in Table 2. Drugs used for prophylaxis against infectious diseases, such as valganciclovir/ganciclovir and trimethoprim-sulfamethoxazole, may also have teratogenic effects, and women should be counselled on the relevant risks while still on these medications.^[40,41]

Recipients of solid-organ transplants usually receive several vaccinations prior to surgery, but SA does not have a national guideline for adult vaccination in general, and there is no SA guideline for vaccination in transplant recipients. International guidelines and recommendations are therefore usually followed.^[60] Women contemplating pregnancy after a transplant should have their vaccination status confirmed, and outstanding vaccinations should be administered as appropriate. Annual influenza and COVID-19 vaccinations should be administered, considering the risks associated with these diseases in both pregnant women and transplant recipients. Live vaccines are contraindicated in pregnancy because of the theoretical risk of congenital infection (however, if inadvertently given during pregnancy, this is not an indication for termination of pregnancy), and are usually contraindicated in transplant recipients given the risk of viral replication in the setting of immunosuppression.^[13] A list of recommended vaccines is provided in Table 3. However, clinicians should be aware that some recommended vaccines are not available in the public sector, and patients may be required to pay for these vaccines. Folic acid and iron supplementation are necessary, as up to 30% of renal transplant patients and 25% of liver transplant recipients may be iron deficient.^[61,62]

Overall, preconception counselling provides valuable information to reduce anxiety and ensure informed decision-making, maximising the chances of a successful pregnancy. Table 3 summarises aspects to be addressed in transplant recipients contemplating pregnancy.

Table 1. Contraceptive methods and their use in kidney or liver transplant recipients^[29-31]

Contraceptive class	Advantages	Disadvantages	Recommendation
Combined hormonal contraception	Reliable Non-contraceptive benefits (cycle regulation, reduced menstrual bleeding)	Daily dosing Increased thrombotic risk Not recommended for women with uncontrolled hypertension or chronic liver disease Not recommended for women with previous myocardial infarction, stroke or VTE	Avoid in complicated graft function Avoid in women with previous or current VTE
Progestogen-only pills	Oestrogen free	Strict daily dosing Requires first-pass liver metabolism	Safe
Copper-containing intrauterine devices	Highly effective (0.8% failure rate) Effective for up to 10 years Reversible	May result in heavy menstruation	Safe
Levonorgestrel-containing intrauterine systems	Highly effective (0.2% failure rate) Effective for up to 5 years Reduces menstrual blood loss Reversible	Irregular menses to amenorrhoea (may be advantageous, depending on the patient)	Safe in uncomplicated grafts Initiate with caution in complicated grafts
Depot medroxyprogesterone acetate	Long acting Reduces menstrual blood loss	Delayed return to fertility (up to 18 months) Decrease in bone mineral density	Safe
Barrier methods	No drug-drug interactions Protects against sexually transmitted diseases	High failure rate	Safe Recommended in addition to other methods

VTE = venous thromboembolism.

The effect of pregnancy on kidney allograft function and outcomes

During normal pregnancy, the glomerular filtration rate (GFR) increases by ~50% with a subsequent reduction in serum urea and creatinine levels. In response to pregnancy-related physiological changes, the kidney allograft adapts with a 30 - 50% increase in creatinine clearance in the first and second trimesters, returning to pre-pregnancy values in the third trimester.^[81] This altered physiology makes close monitoring of drug levels essential, as noted above, because there may be wide fluctuations in the distribution and clearance of drugs.

Pregnant kidney allograft recipients may have less obvious reductions in serum creatinine, with some women having no reduction in the second trimester. In women with no reduction or increased serum creatinine, other potential causes of graft dysfunction should be considered, such as pre-eclampsia, allograft rejection, drug toxicity, volume depletion, obstruction, or urinary tract infection.^[69] Limited data suggest that ultrasound-guided kidney allograft biopsy is safe and well tolerated in pregnancy and may be necessary to determine the cause of graft dysfunction.^[82]

Pregnant kidney transplant recipients have a higher 24-hour protein excretion compared with healthy pregnant women. Proteinuria increases with the duration of pregnancy and may exceed 500 mg/d, returning to pre-pregnancy levels within 8 - 12 weeks after delivery.^[83]

During pregnancy with a well-functioning graft, kidney allograft function is comparable to that of non-pregnant transplant recipients.^[81,84-86] In one study, an accelerated reduction in estimated GFR (eGFR) over time was reported, but no difference in graft loss or reduction of eGFR by >50% over a median of 8 years' follow-up was noted.^[84] Similarly, a meta-analysis noted a small reduction in eGFR within 2 years after delivery, without a risk of long-term graft loss.^[85]

Graft dysfunction, poor blood pressure control and proteinuria prior to pregnancy are the major factors influencing graft function, as well as outcomes during and after pregnancy.^[87] Similarly, blood pressure control and stability of immunosuppressive drug levels during pregnancy are major predictors of graft function. Timing of the

pregnancy is crucial, with the greatest risk of death-censored graft loss (loss of the transplanted organ without death of the recipient) during the first 2 years after transplantation.^[63] Sensitised patients (those who have developed antibodies against their transplanted organ) are also at increased risk of graft rejection during pregnancy.^[88]

The effect of pregnancy on liver allograft function and outcomes

During pregnancy, the placenta produces increased amounts of alkaline phosphatase, resulting in a three- to four-fold rise in this enzyme. However, hepatic synthesis of gamma-glutamyl transpeptidase is reduced. Transaminases remain constant in pregnancy; any increase therefore warrants screening for viral hepatitis (hepatitis A, B and C, and herpesviruses), drug reactions, pregnancy-related factors (such as pre-eclampsia), and toxin ingestion (paracetamol, mushroom poisoning).^[13] In addition, it should be noted that pregnant liver transplant recipients have an increased incidence of intrahepatic cholestasis of pregnancy (ICP) (17% v. 0.5 - 5.6% background risk). Any pregnant woman who has had a liver transplant and presents with pruritus should be investigated for ICP and have bile acid levels measured.^[4,89]

Although liver allograft survival is the same in pregnant and non-pregnant transplant recipients, allograft loss is among the major complications that may occur post-transplant. The incidence of allograft loss is affected by immunosuppressive therapy, age, comorbidities, and allograft function at the time of conception. Despite the low risk of rejection, it remains a threat to the pregnant liver transplant recipient, with the highest incidence seen in the first year after transplantation.^[90] The frequency of acute rejection in pregnancy varies from 0% to 20%,^[13,91-94] while rates of postpartum allograft rejection vary between 3% and 12%.^[13] Local data on rejection in pregnancy are limited to a small study showing two rejection episodes in five pregnancies.^[9] Ultrasound-guided liver biopsy is not contraindicated in pregnancy and should be performed in cases where management may be altered. Pregnant liver transplant recipients with acute rejection during the course of their pregnancy

Table 2. Immunosuppressive drugs commonly used in transplant recipients and their safety in pregnancy

Immunosuppressive drug (drug class)	Notable adverse effects	Safety in pregnancy	Safety in breastfeeding	Dose adjustment in pregnancy
Azathioprine ^[42-45] (antiproliferative agent) Trade names: Azamun, Azapress, Imuran, Zaprine	No major teratogenicity observed May cause anaemia in neonates	Low risk	Low risk	No dose adjustment required Doses ≤ 2 mg/kg safe
Cyclosporine ^[42,45] (calcineurin inhibitor) Trade names: Ciclohexal, Sandimmun	No major teratogenicity observed Increased risk of hypertension, pre-eclampsia, gestational diabetes, fetal growth restriction and preterm birth (appear to be dose related)	Low risk (at lowest effective dose)	Low risk	May require significant dose adjustments (highly bound to albumin, metabolised via CYP450)
Everolimus/sirolimus ^[46] (tyrosine kinase inhibitor) Trade names: Afinitor, Certican (everolimus) Rapamune (sirolimus)	Not enough safety data Reports of adverse fetal effects in animal studies	Not recommended	Not recommended	Switch to an alternative drug if possible
MMF and MPA ^[42,45,47-49] (antiproliferative agent) Trade names: Mycokem, Mycophenolate alkem, Mycophenolate Teva, Micomune, Mycocept, Cellcept, Cimune, Immunolate, Myfortic	Significant adverse effects: High risk of first-trimester miscarriage MMF embryopathy (orofacial clefts, microtia with aural atresia, micrognathia and ocular anomalies), cardiac and spinal abnormalities	Contraindicated	Not recommended	Contraindicated Switch at least 6 weeks prior to attempting conception
Prednisone ^[45,50,51] (corticosteroid) Trade names: Meticorten, Trolac, Panafcort, Pulmison	Limited fetal exposure due to placental 11-beta-hydroxysteroid dehydrogenase Increased risk of gestational diabetes and hypertension	Low risk	Low risk	Maintain on lowest effective dose
Tacrolimus ^[42,45,52] (calcineurin inhibitor) Trade names: Talomune, Prograf, Advagraf, Tacrum, Tarograf	No major teratogenicity observed Limited and confounding data regarding spontaneous miscarriage, congenital malformations and intrauterine death Increased risk of hypertension, pre-eclampsia, gestational diabetes, fetal growth restriction and preterm birth (appear to be dose related)	Low risk	Low risk	May require significant dose adjustments (highly bound to albumin, metabolised via CYP450)
Belatacept ^[53-56] (selective T-cell costimulation blocker) Trade name: Nulojix	Limited data on use in pregnancy (19 cases) No increased risk of adverse pregnancy, maternal or fetal outcomes compared with tacrolimus. No teratogenicity in animal studies at doses 16 - 19 times the recommended human dose	Appears low risk, but data are limited	No data (unlikely to appear in breastmilk given molecular weight)	May require dose adjustments
Basiliximab ^[57-59] (interleukin-2 inhibitor) Trade name: Simulect	Limited data on use in pregnancy No teratogenicity in animal studies, but manufacturer recommends against use in pregnancy and during breastfeeding	Not recommended	Not recommended	Not recommended

MMF = mycophenolate mofetil; MPA = mycophenolic acid; CYP450 = cytochrome P450.

Table 3. Important aspects related to pregnancy in the post-transplant patient considering pregnancy

	Considerations
Contraception	Discuss: <ul style="list-style-type: none"> • The various contraceptive methods available • The indications and contraindications for each method
Timing of conception for kidney and liver transplant recipients ^[4,63,64]	Discuss that: <ul style="list-style-type: none"> • Women should delay conception for at least 1 year (preferably 2 years) post-transplant • Graft function should be stable on an established immunosuppressive regimen • There should be no recent rejection or infectious episodes prior to conception • Teratogenic medication should be discontinued prior to conception (see Table 2)
Management of immunosuppression ^[65,66]	Discuss the need to: <ul style="list-style-type: none"> • Modify immunosuppression to minimise risk to the pregnancy and fetus • Discontinue contraindicated immunosuppressives prior to conception • Monitor drug levels more frequently during pregnancy • Adjust drug dosages as required (see Table 2)
Maternal risks ^[67,68]	Discuss the need for optimisation of comorbid conditions and the increased risks of: <ul style="list-style-type: none"> • Pre-eclampsia • Allograft loss • Gestational diabetes
Fetal outcomes ^[69,70]	Discuss the increased risks of: <ul style="list-style-type: none"> • Preterm delivery • Low birthweight • Caesarean section
Vaccinations ^[71-75]	Administer prior to transplant and/or at least 1 month prior to pregnancy: <ul style="list-style-type: none"> • MMR[†] • Varicella (live)[†]
Availability ^[76-80]	Administer prior to pregnancy: <ul style="list-style-type: none"> • Meningococcus (if in a high-risk group)* Administer prior to or during pregnancy: <ul style="list-style-type: none"> • Seasonal influenza (inactivated)* • COVID-19* • Tdap* • Hepatitis A[‡] • Hepatitis B (if non-immune)*

MMR = measles, mumps, rubella; Tdap = tetanus, diphtheria, pertussis.

* Available in the public health sector.

† Available in South Africa, but not in the public health sector.

are at risk of adverse maternal and fetal outcomes and have an increased risk of subsequent episodes of rejection and allograft loss after delivery.^[4,9]

Women with autoimmune hepatitis are at increased risk of autoimmune recurrence, especially during the postpartum period, so close monitoring of liver function is advised.^[13] Hepatic venous outflow obstruction (in particular Budd-Chiari syndrome) requires further mention, as both local and international guidelines recommend anticoagulation during pregnancy in women with a previous venous thromboembolism (VTE).^[35,95,96] Low-molecular-weight heparin (LMWH) is the preferred agent for anticoagulation in these women. Kidney and liver transplant recipients who have had a VTE at other sites and/or those at risk for VTE from other risk factors should also be anticoagulated with LMWH.^[95,96]

Pregnant liver transplant recipients have high and widely varying rates of hypertensive disorders of pregnancy. This variation is probably influenced by differing inclusion criteria and pre-existing chronic hypertension, with documented rates as high as 43%. Furthermore, the incidence of hypertension varies with differing immunosuppressant regimens, with hypertension being most frequent with the use of cyclosporine (63 - 73%), followed by tacrolimus (47 - 54%) and corticosteroids (22 - 29%).^[13,92] In addition, transplant recipients have increased rates of pre-eclampsia, with newer studies reporting rates of up to 12%.^[13] Similarly, the incidence of gestational diabetes mellitus (GDM) in transplant recipients is higher than in non-transplanted women (8.6 v. 5.4%).^[13,92]

Antenatal management of kidney or liver transplant recipients

Pregnant kidney or liver transplant recipients should be referred for antenatal care as early as possible following confirmation of their pregnancy, for counselling regarding maternal and fetal outcomes, as outlined below. This should take place in a tertiary or central hospital, with access to maternal-fetal medicine and high-risk obstetrics and transplant services, or, in the case of women in the private sector, with an obstetrician or maternal-fetal medicine specialist experienced in managing pregnancy in kidney or liver transplant recipients, with regular multidisciplinary input from the nephrologist or hepatologist, depending on the transplanted organ. Increased rates of pre-eclampsia, GDM, IUGR and preterm labour are seen in this population, and these risks should be discussed.^[13,92]

First trimester

Following confirmation of pregnancy, all women who have undergone organ transplantation should be offered an obstetric ultrasound scan at their first visit, to confirm a viable intrauterine pregnancy and to date the pregnancy accurately. Routine investigations, including haemoglobin, blood typing, syphilis serology and HIV screening, should be done as per national and local protocols.^[97] Anaemia is a particular concern, especially in liver and renal transplant recipients, and appropriate iron and folic acid supplementation should be prescribed.^[98,99]

At 11 - 13 weeks, screening for chromosomal abnormalities through nuchal translucency measurement and biochemical testing should be offered. Serum concentrations of free beta-human chorionic gonadotrophin (beta-hCG) and pregnancy-associated plasma protein A (PAPP-A) are significantly increased in post-transplant pregnancies, and a significant increase in false-positive screening tests for Down syndrome may therefore be seen. Expectant parents should be counselled on the high false-positive rate if biochemical screening is offered.^[100] A risk assessment for pre-eclampsia should also be carried out, and low-dose aspirin should be prescribed as per the 2019 SA national guideline if the woman is at risk.^[101] All women should be screened for GDM because of the increased incidence in transplant recipients, and the first screening should be performed between 12 and 14 weeks, particularly for women on long-term tacrolimus and corticosteroid therapy, rather than the standard 24 - 28 weeks.^[30]

The use of non-invasive prenatal testing (NIPT) has not been well described in this cohort, but NIPT has been described as a possible marker of allograft rejection.^[102] Concerns about incorrect fetal sex determination have been raised following a single case report of discordant sex determination following a liver transplant with a male donor.^[103] NIPT must be undertaken with caution in this setting, and the presence of the graft must be conveyed to the laboratory – any positive result should be followed up with confirmatory testing prior to definitive management.

Additional investigations and interventions for transplant recipients depend on the underlying cause that necessitated the transplant. For instance, women with hereditary diseases such as glycogen storage disorders, Wilson's disease and autosomal dominant polycystic kidney disease may require genetic counselling and testing. Remaining baseline blood tests should be performed as per Box 1. Follow-up in the first trimester should take place every 4 weeks, as opposed to 'basic antenatal care',^[97] which recommends follow-up at 20 weeks only, after the first visit.

Second trimester

During the second trimester, women should be followed up every 2 weeks, as opposed to at 20 and 26 - 28 weeks for basic antenatal care,^[97] alternating with their transplant physician and obstetrician,

with laboratory tests done at each visit as per Box 1. A fetal anatomy scan should be offered at 18 - 22 weeks and a repeat screen for GDM should be done at 24 - 28 weeks. Immunosuppressant drug levels should also be monitored regularly, as set out in Box 1.

Third trimester

Antenatal visits every 2 weeks are recommended until 36 weeks' gestation, as opposed to the visits at 32 - 34, 38 and 41 (if still pregnant) weeks recommended under basic antenatal care.^[97] After 36 weeks, weekly visits should take place until delivery. Fetal biometry and Doppler velocimetry should be assessed every 4 weeks, or more regularly if there are concerns related to fetal growth and/or placental insufficiency. A delivery plan should be discussed with the patient and the MDT. Caesarean section is only recommended for obstetric indications.^[104] The anaesthetic team should be consulted early to plan analgesia at the time of delivery.^[45] Pregnant women on long-term steroid therapy should receive intravenous stress steroids.

Labour, delivery and postpartum management

Delivery planning for recipients of kidney or liver transplants requires a multidisciplinary approach involving specialists in maternal-fetal medicine, obstetric medicine, critical care, transplant medicine, anaesthetics and neonatology. The mode of delivery should be determined based on obstetric indications, and the presence of a donor kidney in the maternal pelvis does not necessarily require a caesarean delivery.^[64,105]

Maternal and fetal/neonatal factors must be considered during delivery planning. Women with kidney or liver transplants are at risk of developing anaemia, as a complication of kidney and liver transplantation is the development of antibodies against recipient red blood cells, arising from transplanted organs.^[98,99] Regular anaemia assessments are therefore necessary, with assessment and treatment of the underlying cause as appropriate. Cross-matching should be requested ahead of time to anticipate the need for blood and/or blood products. Additionally, the incidence of pre-eclampsia is as high as 30% in transplant recipients, which can complicate the intrapartum and postpartum periods, requiring increased surveillance.^[106]

Given the immunosuppressed state of women with kidney and liver transplants, meticulous aseptic techniques should be practised during all procedures, especially at urinary catheterisation and operative vaginal and caesarean deliveries.^[107] During the postpartum period, careful monitoring for postpartum haemorrhage and VTE is necessary, as these complications may be more common in post-transplant women.^[108,109] VTE prophylaxis, including mechanical and pharmacological measures, should be individualised and initiated appropriately.^[109]

Antenatal discussions should address breastfeeding and the potential risks and benefits thereof for post-transplant women. There is some debate regarding breastfeeding in women who have had an organ transplant.^[93] While some immunosuppressant drugs are not recommended during breastfeeding, an increasing number of women are choosing to breastfeed while on immunosuppression. Data from the TPRI show that the rate of breastfeeding in women post-transplant increased from 10% in 2000 to ~70% in 2020.^[4] Current data suggest that azathioprine, cyclosporine, prednisone and tacrolimus are safe during breastfeeding, whereas mycophenolate mofetil, sirolimus and everolimus are not recommended.^[4] Immunosuppressive drug levels should be closely monitored during pregnancy and during the 3 months postpartum owing to changes in volume of distribution, metabolism, and drug binding capacity.^[30,93]

Box 1. Recommended laboratory tests in pregnant transplant recipients

Booking

- Routine antenatal tests (blood group, syphilis serology and HIV)
- Full blood count
- Urea, creatinine and electrolytes
- Liver function tests
- Tacrolimus and cyclosporine drug levels (as appropriate)
- Viral hepatitis serology – A, B and C
- Cytomegalovirus, toxoplasmosis, rubella

During pregnancy

- Monthly haemoglobin (and platelets if indicated, e.g. in women with portal hypertension)
- Monthly urea and electrolytes or liver function tests (depending on transplanted organ)
- Monthly immunosuppressant drug levels until 32 weeks, then 1 - 2-weekly
- Monthly urine microscopy and culture (in renal transplant recipients)

Postpartum

- Immunosuppressant drug levels 1 week postpartum

As noted above, contraceptive counselling and timing are crucial for a smooth transition out of the puerperium. Permanent contraceptive methods may be considered if fertility is no longer desired. Screening and counselling for maternal mental health disorders and postpartum depression are also recommended.

Neonatal and paediatric outcomes

While SA data on neonatal and paediatric outcomes in children born to kidney or liver transplant recipients are lacking, it is clear from the international literature that pregnancy after a transplant carries an increased risk of neonatal complications. In a UK national cohort study, more than half (52%) of kidney transplant recipients delivered preterm (before 37 weeks' gestational age), compared with the national average of 8%.^[69] The risk of being born before 32 weeks' gestational age is four times higher in babies born to mothers who have had a solid-organ transplant compared with national data.^[69] Although rates of prematurity in liver transplant recipients are lower than in kidney transplant recipients, they are still four times greater than in the general population.^[6] Intrauterine growth restriction is more common in kidney transplant recipients, and there is a greater risk of the baby being born with a low birthweight (<2 500 g).^[69,70] However, growth appears to be similar to that of the general population after 1 year of age.^[110]

The risk of congenital anomalies is also increased in neonates born to women who have had a solid-organ transplant, although the exact risk is difficult to quantify owing to the small numbers in most reports.^[69,70] A Danish study found the risk to be double that of the matched control cohort.^[70] The increased risk of congenital anomalies may be due to fetal exposure to teratogenic immunosuppressive drugs, or to maternal age and comorbidities (such as hypertension or diabetes).^[111]

After birth, neonates born to transplant recipients have an increased need for intensive care, mostly due to complications of prematurity. Delivery should therefore take place with suitably trained staff in attendance and neonatal support readily available.^[69] Infants born to transplant recipients appear to have alterations in immune cell numbers and an increased rate of hospitalisation due to infection.^[110] Reassuringly, no significant differences in infant mortality (death during the first year of life) were noted, and vaccine response appears not to be affected.^[70,110] A recent systematic review analysing long-term outcomes (beyond the first year of life) in 1 664 children born to women after a solid-organ transplant (78% kidney and 17% liver transplants) has also been reassuring, with no alterations in growth, neurocognitive function, behavioural development or antibody response compared with the general population. However, a possible increase in the risk of infection was noted in children born to kidney transplant recipients, with more infectious disease-related hospitalisations compared with controls, and a significantly higher number of antibiotic prescriptions in children aged 1 - 5 years.^[110] Long-term follow-up is recommended for children born to transplant recipients to assess any potential long-term effects of fetal exposure to immunosuppressive drugs.

Conclusion

Pregnancy after kidney or liver transplantation requires careful planning and management to ensure optimal outcomes for both mother and baby. A multidisciplinary approach involving obstetricians, maternal-fetal medicine specialists, transplant and obstetric physicians, anaesthetists, neonatologists and other specialists is necessary to manage the complex medical issues associated with these pregnancies. Close monitoring of maternal and fetal wellbeing, as well as immunosuppressive drug levels, is essential

throughout pregnancy and the postpartum period. While these pregnancies are associated with an increased risk of complications such as prematurity, low birthweight and congenital anomalies, early detection and appropriate management can improve outcomes for both mother and baby. Further research into the outcomes of pregnancies in women with kidney and liver transplants in the SA setting is required. We recommend the establishment of a local registry to assess outcomes in these women and their infants.

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