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Pregnancy in Kidney and Liver Transplant Recipients: Maternal and Fetal Risks and Management Challenges - narrative review

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Abstract

Background. The rising success of SOT among younger patients has made pregnancy an increasingly viable reality. However, these cases remain inherently high-risk, requiring a delicate clinical balance between maintaining graft stability, ensuring maternal safety and supporting fetal development.

Aim. This review synthesizes current evidence regarding pregnancy management and outcomes in kidney and liver transplant recipients, focusing on clinical strategies to optimize maternal and neonatal health.

Material and methods. A systematic search was conducted across PubMed, Scopus, and Google Scholar. The analysis included randomized trials, systematic reviews and clinical guidelines published in English, with a focus on high-quality, recent evidence.

Results. SOT typically restores fertility within 6–12 months post-transplant, yet pregnancies in this cohort are frequently complicated. Maternal risks are dominated by hypertensive disorders, which occur at significantly higher rates than in the general population. Fetal outcomes are primarily impacted by preterm birth, leading to higher incidences of low birth weight and intrauterine growth restriction. Success hinges on a multidisciplinary approach and the strict optimization of immunosuppression. Current protocols emphasize the mandatory transition from teratogens to safer alternatives, such as Tacrolimus. However, altered pharmacokinetics during pregnancy necessitate proactive serum monitoring and dosage adjustments to compensate for accelerated drug clearance.

Conclusions. While transplant pregnancies are complex, favorable outcomes are achievable through meticulous, multidisciplinary care. Key success factors include the avoidance of teratogens and rigorous monitoring of both blood pressure and drug levels. When managed proactively, most recipients can achieve successful gestational results without compromising long-term graft survival. Continued research remains essential to further refine these high-risk protocols.

Key words: pregnancy, solid organ transplantation, maternal outcomes, fetal outcomes, kidney transplantation, liver transplantation

1. Introduction

The history of pregnancy in transplant medicine began in 1958, with the first successful birth reported in a kidney transplant recipient who had received a graft from her identical twin (1). A significant milestone followed in 1963, marking the first successful pregnancy maintained under an immunosuppressive regimen consisting of corticosteroids and azathioprine (2). The field of transplant obstetrics underwent another major shift in the early 1980s when cyclosporine was introduced (3,4). This advancement allowed for the development of more effective management strategies and expanded the possibility of motherhood to recipients of other organs. Consequently, the first successful pregnancies were reported following liver transplantation in 1978 and heart transplantation in 1988 (5,6). The field of transplant obstetrics is undergoing rapid evolution, characterized by continuous advancements in surgical techniques and the development of novel immunosuppressive agents. Given these rapid clinical advancements, continuous integration of the latest evidence is crucial for optimizing the care of this multifaceted patient group. Precise, evidence-based protocols are required to balance the requirements of graft stability with the physiological demands of pregnancy.

The primary objective of this review is to synthesize current evidence regarding pregnancy outcomes in solid organ transplant recipients and to provide a comprehensive overview of the associated clinical challenges. This study specifically addresses the primary maternal and fetal risks associated with pregnancy across various types of solid organ transplantation, including kidney and liver. It further explores the influence of modern immunosuppressive protocols on long-term graft survival and the specific risks of congenital malformations. Furthermore, this review highlights the primary clinical complications managed by multidisciplinary teams, providing insights that may help standardize protocols and improve outcomes for these high-risk pregnancies. It is hypothesized that while pregnancy in transplant recipients carries a higher risk of complications such as preeclampsia and preterm birth, optimized pharmacological management and multidisciplinary care allow for favourable outcomes without compromising the stability of the allograft.

2. Research materials and methods

The literature search was performed across three major electronic databases: PubMed, Scopus, and Google Scholar. The search focused on publications from the last 15 years (2011–2026) to ensure a focus on modern immunosuppressive protocols and the most recent clinical outcomes. Earlier publications were consulted exclusively for historical context

regarding the evolution of transplant obstetrics. The following keywords and their combinations were utilized: "pregnancy," "solid organ transplantation," "graft survival," "kidney transplantation," "liver transplantation," "fetal outcomes," and "maternal outcomes." Boolean operators (AND, OR) were applied to refine the search and maximize the relevance of the results. Inclusion criteria encompassed retrospective studies, cohort studies, reviews, systematic reviews, guidelines and randomized controlled trials. Exclusion criteria included case reports, conference abstracts, papers without full text, non-English publications, duplicate records, and studies not directly related to pregnancy in solid organ transplantation recipients.

This review relies on the statistical findings reported in the original studies and meta-analyses. Consequently, no independent data synthesis or statistical re-analysis was performed, and no specialized statistical software was utilized.

AI tools were used strictly for linguistic editing and grammatical refinement to ensure clarity and adherence to academic writing standards. All analytical processes, data interpretation, and conclusions were conducted exclusively by the human authors without AI intervention in the research findings.

3. Research results

3.1. Kidney transplantation

According to the 2024 report from the Global Observatory on Donation and Transplantation, kidney transplantation remains the most frequently performed solid organ procedure worldwide. Kidney transplantations accounted for 110,467 cases, representing roughly 63.6% of all procedures (7).

For women of childbearing age, the significance of this procedure extends beyond life expectancy. End-stage renal disease is frequently complicated by infertility, primarily due to severe disruptions in the hypothalamic-pituitary-gonadal axis. These hormonal imbalances and the resulting insufficiency of sex hormones create significant barriers to conception. However, successful transplantation offers an intervention for these reproductive issues. With the recovery of kidney function, the endocrine environment typically stabilizes in a relatively short timeframe, often returning to baseline within six months of the procedure. Consequently, for

women facing ESRD, a kidney transplant often represents the most viable path toward a successful pregnancy (8).

Establishing the appropriate interval between transplantation and conception is a critical clinical decision that requires a thorough assessment of maternal health and allograft stability. Current consensus from the American Society of Transplantation suggests that recipients should generally delay pregnancy for at least one year following a successful transplant. This indicates a significant evolution beyond the outdated European Best Practice Guidelines, which recommended a more conservative two-year waiting period. This transition toward a shorter interval reflects advancements in immunosuppressive strategies that have effectively reduced the incidence of early acute rejection. Despite these general benchmarks, the timing of pregnancy must be determined on an individual basis, ensuring that several strict clinical criteria are satisfied to protect both the mother and the graft. A candidate for pregnancy must demonstrate optimal allograft function, typically defined by a stable serum creatinine level of less than 1.5 mg/dL (133 μ mol/L) and the absence of significant proteinuria and well controlled hypertension or normal blood pressure. It is also essential that the patient has not experienced any acute rejection episodes within the preceding year and is maintained on a stable dose of immunosuppression (9,10).

Evidence suggests that while conceiving within two years of transplantation significantly elevates the risk of hypertension and preeclampsia, it does not appear to worsen other perinatal outcomes. Their findings suggest that patients who chose to become pregnant before the two-year mark did not experience a significant increase in the rates of preterm birth, low birth weight, or premature rupture of membranes. Furthermore, the study noted that early pregnancy was not associated with a higher incidence of maternal infections or long-term graft dysfunction (11).

Clinical data highlights that pregnancy in solid organ transplant recipients involves a high frequency of obstetric interventions and medical complications. The most prevalent maternal outcome is delivery via caesarean section, occurring in 68.67% of cases. This rate is approximately twice as high as that observed in the general U.S. population. Hypertensive disorders constitute a significant clinical challenge in the management of this patient population. Chronic hypertension is particularly prevalent, affecting an estimated 52–69% of recipients even before conception. Pregnancy-induced hypertension is reported in 24.30% of

recipients, while preeclampsia affects 20.87%. Notably, the risk of developing preeclampsia in renal transplant recipients is estimated to be six times higher than in the general population. Other frequently encountered complications include urinary tract infections and anaemia, both of which require proactive screening and management throughout the gestational period (12–15). In contrast to hypertensive risks, the incidence of gestational diabetes in renal transplant recipients ranges from 3% to 8%. This rate is generally considered comparable to that of the normal population (16). Fetal outcomes and long-term graft stability are central concerns in transplant obstetrics. Evidence from meta-analyses indicates that solid organ transplantation is strongly associated with an increased risk of adverse neonatal outcomes. Specifically, transplantation is linked to a significantly higher likelihood of low birth weight, with an OR of 5.50. Furthermore, the risk of preterm birth is substantially elevated in this population, showing an even stronger association with an OR of 7.48 (17).

Regarding maternal health, the outlook for graft survival is generally encouraging. In patients with a well-functioning graft before conception, kidney allograft performance during pregnancy remains comparable to that observed in non-pregnant transplant recipients. While some meta-analyses have noted a minor reduction in the estimated glomerular filtration rate within the first two years following delivery, this decline does not appear to translate into an increased risk of long-term graft loss. When pre-gestational organ function is well-maintained, the majority of transplant patients do not experience a decline in graft longevity, despite the significant hemodynamic stress associated with pregnancy (18,19).

3.2. Liver transplantation

Following kidney transplantation, liver transplantation represents the second most frequent solid organ procedure performed globally. According to current international data, LTx accounts for 42,497 documented procedures, representing approximately 24.5% of the total global transplant volume across 71 reporting countries (7).

In women suffering from advanced liver disease, infertility is frequently driven by significant hormonal imbalances, including altered estrogen metabolism and a fundamental disruption of the hypothalamic-pituitary-gonadal axis. These disturbances, characterized by suppressed levels of FSH and LH, typically lead to chronic anovulation and amenorrhea (20).

However, the restoration of hepatic function through transplantation often acts as a definitive treatment for these reproductive issues. Most recipients experience a rapid return of regular menses within the first-year post-transplant, though it is noteworthy that ovulation and the potential for conception can resume as early as the first month after the procedure (21,22).

Although fertility can return remarkably fast after liver transplantation, the American Society of Transplantation emphasizes a cautious approach to family planning. Current guidelines generally recommend that recipients postpone pregnancy for a minimum of one year following the procedure. This interval is vital for establishing clinical stability, as it provides the multidisciplinary team with sufficient time to monitor for any recent rejection episodes and ensure the graft is functioning reliably. Furthermore, this period allows for the effective management of opportunistic infections, such as cytomegalovirus and the careful titration of maintenance immunosuppressive regimens to the lowest effective doses before conception (10).

Supervised by a specialized multidisciplinary team, the overall clinical outcomes are encouragingly positive. Pregnancy in liver transplant recipients involves a correlation of maternal and fetal risks, with pregnancy-induced hypertension, pre-eclampsia and intrauterine growth restriction being the most significant concerns (23). Research indicates that liver transplant recipients present with more severe clinical profiles. The incidence of fetal mortality, antepartum hospitalizations, and general maternal or fetal complications is two to three times higher than in the general population. Research by Coffin et al. highlighted this disparity, noting a 30% PIH rate among LT recipients compared to just 9% in healthy controls (24). It is also significant that LT recipients generally experience fewer hypertensive complications compared to kidney transplant recipients, who face a substantially higher prevalence, often cited at 54% (25). The literature indicates that pre-eclampsia rates have stabilized between 7% and 12%, though it remains the primary clinical driver of preterm delivery in this population (26–29). Beyond cardiovascular concerns, metabolic complications such as gestational diabetes present a notable challenge. Evidence from a large-scale American population-based study indicates that LT recipients face a significantly higher risk of developing GD with an incidence rate of 8.6% compared to 5.4% in the non-transplant control group (30). Haemorrhagic complications also require careful attention. While antepartum haemorrhage rates remain similar to those of the general population, the risk of postpartum haemorrhage is statistically higher in LT recipients, occurring in 8% of cases compared to 3% in controls. This may be linked to the higher frequency of surgical interventions and the underlying effects of chronic

immunosuppression(24).Fetal outcomes reflect the high-risk nature of these gestations. Systematic reviews indicate a spontaneous abortion rate of approximately 8%. Prematurity remains a significant challenge with recent reviews reporting an incidence of approximately 30%(36). Furthermore, IUGR is significantly more frequent in this population. Deshpande et al. found that 45% of infants born to LT recipients were affected by growth restriction, compared to the 32% rate observed in the general U.S. population (25).

Regarding graft stability, rejection during pregnancy is highly variable, with reported rates ranging from 0% to 20%. In the postpartum period, this risk persists at a level of 3% to 12%, necessitating rapid adjustments to medication levels after delivery (31–35).

3.5 Immunosuppressive treatment

Managing a successful pregnancy in transplant recipients depends on maintaining consistent immunosuppressive therapy to safeguard both maternal and fetal health. Adherence to the prescribed therapeutic regimen is essential for maintaining graft function and preventing autoimmune exacerbations, as suboptimal dosing or treatment discontinuation may result in serious adverse outcomes, including irreversible graft loss. Most conventional immunosuppressive agents, including prednisone, azathioprine, cyclosporine, and tacrolimus, are regarded as relatively safe for use during pregnancy, as they do not appear to increase the baseline risk of congenital malformations. In contrast, exposure to mycophenolic acid presents a significantly different risk profile. Data from the National Transplantation Pregnancy Registry indicates that MPA exposure is strongly linked to a higher frequency of spontaneous abortions (48%) and a 24% incidence of structural birth defects and fetal abnormalities. Consequently, MPA is strictly contraindicated and patients should be transitioned to safer alternatives at least six weeks before attempting conception(37–39).Currently, tacrolimus serves as a cornerstone of transplantation medicine. The pharmacokinetics of tacrolimus are significantly altered by the physiological changes of pregnancy. Factors such as increased volume of distribution and heightened CYP3A4 enzyme activity often result in lower systemic drug levels. To maintain a therapeutic trough range, typically between, depending on the indication, pregnant patients often require higher oral doses (40–42). The Society for Maternal-Fetal Medicine recommends monitoring tacrolimus serum levels at least every four weeks during the first two trimesters, increasing the frequency to every one to two weeks after the 32nd week of gestation as delivery approaches. Immediately

following childbirth, pre-pregnancy dosages should be reinstated to avoid toxicity, with drug levels checked within the first week postpartum. Additionally, serial ultrasounds are suggested starting at 24–28 weeks to monitor fetal growth in patients receiving tacrolimus (43).

4. Conclusions

The evolution of transplant medicine has transformed pregnancy from a contraindicated risk into a viable clinical reality for organ recipients. This review confirms that while these pregnancies are inherently high-risk, favourable outcomes for both the mother and the newborn are achievable through a meticulously coordinated, multidisciplinary approach. To ensure that maternal and fetal outcomes remain satisfactory, it is imperative to strictly adhere to current clinical guidelines and evidence-based protocols.

Current evidence suggests that the timing of pregnancy should be delayed for at least one year following a successful transplant to ensure graft stability and the achievement of maintenance immunosuppression. Preeclampsia remains the most significant maternal challenge in this population, as it is a condition that can precipitate preterm birth or progress to eclampsia, carrying severe risks for maternal health. Consequently, rigorous blood pressure control and frequent monitoring are essential components of antenatal care. Pregnancy-induced hypertension is remarkably prevalent, appearing at a rate three times higher in liver transplant recipients than in healthy controls, while in the kidney transplant population, hypertension affects approximately half of all recipients.

The selection of appropriate immunosuppressive agents is critical for the safety of the developing fetus. Specifically, mycophenolate mofetil is strictly contraindicated due to its high association with spontaneous abortions and structural birth defects. Conversely, tacrolimus has become the cornerstone of modern immunosuppressive treatment in organ recipients during pregnancy. While many questions regarding the long-term optimization of outcomes remain unanswered and ethical constraints make randomized clinical trials difficult to implement, a successful pregnancy is certainly possible. Achieving this requires integrated care, necessitating close collaboration between obstetric and transplant specialists to ensure maternal and fetal safety.

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