14. Pregnancy and transplant

14.1 Immunosuppression/therapeutic drug monitoring

de Lima Moreira F, et al. (2023). Optimizing Therapeutic Drug Monitoring in Pregnant Women: A Critical Literature Review. Ther Drug Monit. Epub ahead of print. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36127797/

- Systematic review of studies evaluating therapeutic drug monitoring for various drug classes in pregnant women, including a section on immunosuppressive medications.

Kant S, et al. (2022). Principles of Immunosuppression in the Management of Kidney Disease: Core Curriculum 2022. Am J Kidney Dis. 80(3): 393-405. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35440396/

- This chapter of the Core Curriculum in Nephrology summarizes the various classes of immunosuppression and includes a section on pregnancy. Calcineurin inhibitors, antimetabolites, glucocorticoids, and B-cell-depleting agents are reviewed with recommendations provided for management during pregnancy.

Donovan R, et al. (2022). Antiproliferatives and Transplantation. HandB Exp Pharmacol. 272: 39-52 Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34697667/

- This chapter summarizes the available literature about antiproliferative medication and has a section on pregnancy. Azathioprine can be used safely in pregnancy while mycophenolate is not appropriate for women who are pregnant or planning to be. The negative effects of mycophenolate are not seen in male patients.

Akiyama S, et al. (2022). Pregnancy and neonatal outcomes in women receiving calcineurin inhibitors: A systematic review and meta-analysis. Br Clin J Pharmacol. 88: 3950-3961 Retrieved from: https://pubmed.ncbi.nlm.nih.gov/355593302/

- Systematic review and meta-analysis about calcineurin inhibitor use in pregnant women and neonates. Indications for calcineurin inhibitor use are expanded beyond solid organ transplant. The main adverse effect seen with this drug class in this population was preeclampsia, which causes an increased risk of low birth weight and prematurity. Blood pressure should be monitored carefully throughout pregnancy and ideally well-controlled prior to conception.

Gong X. et al. (2021). Pregnancy outcomes in female patients exposed to cyclosporin-based versus tacrolimus-based immunosuppressive regimens after liver/kidney transplantation: A systematic review and meta-analysis. J Clin Pharm Ther. 00: 1-10. Retrieved from: https://onlinelibrary.wiley.com/doi/10.1111/jcpt.13340

- Systematic review of 10 observational studies (n=1080) showed that tacrolimus-treated recipients experienced lower risk of gestational hypertension. However, cyclosporin-treated recipients showed lower incidence of C-section and had better live birth rate. There were no differences in pre-eclampsia, gestational diabetes, preterm delivery, or birth weight.

Boulay H, et al. (2021). Maternal, fetal and child consequences of immunosuppressive drugs during pregnancy in women with organ transplant: a review. Clinical Kidney Journal. ePub ahead of print Retrieved from: https://academic.oup.com/ckj/advance-article/doi/10.1093/ckj/sfab049/6157850

- Review article summarizing existing data on maternal and fetal complications of pregnancies in women after renal transplant with the focus on both induction and maintenance immunosuppression. From this article, children exposed in utero to azathioprine, calcineurin inhibitors and/or corticosteroids did not present with major congenital defects. The author concluded that pregnancy is associated with risks of preterm birth, preeclampsia, and low birthweight. Pregnancy must be carefully planned and closely monitored by the multidisciplinary healthcare team.

Le HL, et al. (2020). Usage of tacrolimus and mycophenolic acid during conception, pregnancy, and lactation, and its implications for therapeutic drug monitoring: A systematic critical review. Ther Drug Monit. 42(4), 518-531. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32398419/

- Systematic review through August 2019 including 163 studies. Authors concluded tacrolimus treatment during conception, pregnancy, and lactation seems to be relatively safe. Due to pharmacokinetic changes during pregnancy, a higher tacrolimus dose might be indicated to maintain target concentrations. MPA treatment in men during conception seems to have no adverse effect on pregnancy outcomes, whereas MPA use in women during conception and pregnancy is strongly discouraged.

Yuksel Y, et al. (2019). Use of tacrolimus during pregnancy after kidney transplantation. Transplant Proc. 51(7), 2361-2366. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31402247/

- Retrospective study of 26 patients who used tacrolimus during their pregnancies after renal transplantation at a single center from 2008 to 2018. Authors recommend waiting at least 2 years after the renal transplant when graft function should be normal and without any signs of hypertension and proteinuria.

Al-Otaibi T, et al. (2019). Pregnancy after renal transplant: Single center experience from the Middle East in patients using different calcineurin inhibitors. Exp Clin Transplant. 17(1), 99-104. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30777531/

- Case control study of patients who became pregnant between 2004 and 2017. Pregnancies were divided into those who received cyclosporine and those who received tacrolimus. There were no differences in outcomes or complications between the two groups.

Chandra A, et al. (2019). Immunosuppression and reproductive health after kidney transplantation. Transplantation, 103(11), e325-e333. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31397802/

- Review of issues regarding immunosuppression and reproductive health in kidney transplant recipients.

Casale M, et al. (2016). Pharmacologic considerations for solid organ transplant recipients who become pregnant. Pharmacotherapy, 36 (9), 971-82. Retrieved from: https://accpjournals.onlinelibrary.wiley.com/doi/full/10.1002/phar.1800

- Review article in which the authors discuss pharmacokinetic and pharmacodynamic changes in pregnancy and the implications on use of immunosuppression agents. Literature outlining outcome data and treatment trends are also reviewed. The authors conclude with a suggested approach to immune suppression management in the pregnant transplant recipient.

Kim H, et al. (2015). The optimal therapy of calcineurin inhibitors for pregnancy in kidney transplantation. Clinical Transplantation, 29(2):142-8. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/25560652

- Single center retrospective cohort evaluating the effect of pregnancy on renal function in kidney transplant recipients (n=75) and changes in calcineurin inhibitors drug concentrations and dose requirements during gestation. Generally serum creatinine returned to pre-pregnancy baseline following delivery. The authors observed a decrease in both tacrolimus and cyclosporine levels during pregnancy requiring dose increases of 20-25% for each agent to maintain levels within the defined therapeutic range.

Paziana K, et al. (2013). Ciclosporin use during pregnancy. Drug Safety, 36 (5), 279-94. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=10.1007%2Fs40264-013-0034-x

- Systematic review of literature evaluating cyclosporine use in pregnancy. The review explores cyclosporine pharmacokinetic and pharmacodynamic changes in pregnancy. The authors also examine cyclosporine use in pregnancy for different solid organ transplant populations among other indications for cyclosporine.

Hebert MF, et al. (2013). Interpreting tacrolimus concentrations during pregnancy and postpartum. Transplantation, 95 (7), 908-15. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/23274970

- This review article looks at tacrolimus pharmacokinetic changes during pregnancy. Discusses factors that influence interpretation of trough concentrations as well as the effect of tacrolimus on the fetus.

Zheng S, et al. (2012). Pharmacokinetics of tacrolimus during pregnancy. Therapeutic Drug Monitoring, 34 (6), 660-70. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/23007747

- Pharmacokinetic study with pregnant women (n=10) drawing tacrolimus levels during early (10-14 weeks gestation), mid (22-26 weeks gestation) and late pregnancy (34-38 weeks gestation). Patients included five kidney, one kidney/pancreas, three liver and one heart transplant recipients. CYP3A5 genotyping verified all subjects were non-expressers. Tacrolimus clearance and whole blood concentrations were compared during pregnancy using postpartum as a reference group. Mean oral clearance of tacrolimus was 39% higher during mid and late pregnancy. Free fraction of tacrolimus increased by 91% in plasma and by 100% in whole blood during pregnancy, inversely associated with albumin, α1-acid glycoprotein, hematocrit and red blood cell concentrations. The authors demonstrated that adjusting tacrolimus dose during pregnancy to maintain the same whole blood concentration results in increased unbound (active) tacrolimus levels and area under the curve during pregnancy (112% and 173%, respectively).

The authors identified a need to reduce goal tacrolimus trough levels during mid-late pregnancy in order to avoid supratherapeutic exposure.

Khan AA, et al. (2011). Does in utero exposure to synthetic glucocorticoids influence birthweight, head circumference and birth length? A systematic review of current evidence in humans. Paediatric and Perinatal Epidemiology, 25 (1), 20-36. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/21133966

- Systematic review evaluating exposure to synthetic glucocorticoids during gestation and associations with birth size. The authors concluded the limited data available suggests a trend in decreased birth weight, head circumference and birth length among infants exposed to glucocorticoids during gestation compared to those who were not.

Petri M. (2003). Immunosuppressive drug use in pregnancy. Autoimmunity, 36 (1), 51-6. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/12765471

- Review of the use of immunosuppressive agents in pregnancy. While the focus of the review in on autoimmune conditions, the summaries include corticosteroids, azathioprine, mycophenolate, and cyclosporine. For each agent, the authors highlight maternal and fetal concerns, placental transfer and excretion into breast milk.

Armenti, VT. (1998). Drug safety issues in pregnancy following transplantation and immunosuppression: effects and outcomes. Drug Safety, 19 (3), 219-32. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/9747668

- Review article integrating National Transplantation Pregnancy Registry data with available literature from the time to outline safety concerns with outcome data. Corticosteroids, azathioprine, cyclosporine, tacrolimus and mycophenolate are reviewed in detail and recommendations for immune suppression management in pregnancy with each agent is offered.

14.2 Lactation

McKinzie C, et al. (2022). Outcomes of children with fetal and lactation immunosuppression exposure born to female transplant recipients. Paediatr Drugs. 24: 483-497. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35870080/

- Maternal use of immunosuppressants should not preclude the use of breastmilk. Utilizing relative infant dose estimations, most commonly used immunosuppressants are likely safe during breastfeeding. Early effects of immunosuppression appear to be short lived but may predispose infants to an increased risk of infectious complications due to decreased circulating immune cells.

Kociszewska-Najman B, et al. (2020). Low Content of cyclosporine A and its metabolites in the colostrum of post-transplant mothers. Nutrients, 12(9). Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7551077/

- Cyclosporine measured in colostrum of seven post-transplant mothers. Researchers found low levels of cyclosporine in the mothers' colostrum. Researchers conclude a need for future studies with more participants and for a longer duration of study time.

Lazar K, et al. (2020). Human cytomegalovirus reactivation during lactation: Impact of antibody kinetics and neutralization in blood and breast milk. Nutrients, 12(2). Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32012818/

- Human cytomegalovirus (HCMV) reactivation occurs and HCMV-specific-IgG is present in breast milk. The role HCMV-IgG neutralizing capacities was explored, but specific role in decreasing HCMV shed in breast milk remains elusive.

Chandra A. et al. (2019). Immunosuppression and reproductive health after kidney transplantation. Transplantation, 103(11), e325-e333. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31397802/

- Review article of contraception counseling points after kidney transplant with a focus on immunosuppressant management in pregnancy and breastfeeding.

Paizis K. (2019). Immunomodulatory drugs in pregnancy and lactation. Aust. Prescr. 42(3), 97-101. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6594853/

- Article discusses changes, monitoring, and medication adjustments (for pregnancy/breastfeeding) for azathioprine and mycophenolate.

Ryu, RJ, et al. (2018). Prednisone pharmacokinetics during pregnancy and lactation. J. Clin. Pharmacol. 58(9), 1223-1232. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29733485/

- Researchers reviewed prednisone use in pregnancy, a drug used to prevent transplant rejection in past recipients of a solid organ transplant. Discussed are the pharmacokinetics of prednisone (and its metabolite prednisolone) during pregnancy and the postpartum period. There is dose-dependent pharmacokinetics of prednisone during pregnancy, but because prednisolone remains unbound, a change in prednisone dose is usually not warranted. Low concentrations of prednisone and prednisolone appear in breast milk; oral prednisone is compatible with breastfeeding. Researchers acknowledge there is a need for additional research (with a larger sample size) to confirm results from this study on pharmacokinetics and pharmacodynamics of prednisone in pregnancy and postpartum.

Bramham K. et al. (2013). Breastfeeding and tacrolimus: serial monitoring in breast-fed and bottle-fed infants. Clinical Journal of the American Society of Nephrology, 8 (4), 563-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/23349333

- The aim of the study was to assess neonatal exposure to tacrolimus from breast milk, through evaluation of maternal trough levels (n=14), infant blood samples (n=15), and breast milk concentrations. Of the infants included, twelve were breastfed and 3 were bottle-fed. Serial blood measurements for each infant were gathered as able. Blood from umbilical cord post delivery was collected in 6 cases. Average maternal blood tacrolimus concentration at delivery was 6.6 mcg/L (range 4.6-11.2 mcg/L). Average umbilical cord blood tacrolimus concentration at delivery was 4.6 mcg/L (range 1-9 mcg/L). Breastfed infant blood tacrolimus concentration average (24 samples) was 1.3 mcg/L (range 0-4 mcg/L) compared with bottle fed infant blood tacrolimus concentration average (6 samples) of 1 mcg/L (range 0-2.3 mcg/L). Average breast milk tacrolimus concentration was 0.8 mcg/L (range 0.1-1.6 mcg/L). Infants with serial blood samples showed a rapidly decreasing concentration with each day post delivery leading the authors to conclude the tacrolimus exposure is due to gestation rather than delivery through breast milk. Based on the highest documented breast milk tacrolimus concentration, the authors estimated the infants tacrolimus dose from breast milk is 0.56 mcg per day (assuming 0.15 L/kg/day breast milk ingestion, infant weight of 2.4 kg).

Thiagarajan KM. et al. (2013). Safety considerations: breastfeeding after transplant. Progress in Transplantation, 23 (2), 137-46. Retrieved from:

- https://www.ncbi.nlm.nih.gov/pubmed/23782661

- Review of available literature outlining safety of breastfeeding after transplant. The authors address the physiology of breast milk production, summarize literature for each immunosuppressive agent and reference National Transplantation Pregnancy Registry data to support immune suppression lactation recommendations for clinicians.

Zheng S. et al. (2013). Tacrolimus placental transfer at delivery and neonatal exposure through breast milk. British Journal Clinical Pharmacology, 76 (6), 988-96. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/23528073

- Pharmacokinetic study in eight solid organ transplant recipients (4 kidney, 1 kidney/pancreas, 1 kidney/heart, and 2 liver) to measure infant tacrolimus exposure during gestation through maternal tacrolimus blood concentrations and umbilical cord concentrations. Average umbilical cord blood tacrolimus concentration was 6.6 ± 1.8 ng/mL while average maternal blood tacrolimus concentration was 9 ± 3.4 ng/mL at the time of delivery. Most tacrolimus levels were collected within 6 hours of taking the dose. Unbound tacrolimus concentration in the umbilical cord were one-fifth of maternal concentrations.

Singh M. et al. (2011). Is breastfeeding safe with azathioprine? Obstetric Medicine, 4 (3), 104-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989605/

- Observational case series including 10 mother-baby pairs to examine the effects of breastfeeding while taking less than 2 mg/kg/day of azathioprine. Infants were taken regularly to be examined by a pediatrician, complete blood counts were collected to detect bone marrow suppression, mothers were instructed to report any illness their child experienced and completed questionnaires regularly to assess frequency of breastfeeding. The authors did not appreciate any major difference in blood counts or infectious complication in the infants studied compared to the general population. Of note, none of the mothers studied were transplant recipients.

Osadchy A. et al. (2011). Cyclosporine and lactation: when the mother is willing to breastfeed. Therapeutic Drug Monitoring, 33 (2), 147-8. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Cyclosporine+and+Lactation%3A+When+the+Mother+Is+Willing

- This is a case report about a renal transplant recipient who continued breastfeeding while on cyclosporine. Drug levels were measured in blood samples from the mother and baby as well as in breast milk in order to justify safety of continuation of breastfeeding while on cyclosporine.

Nyberg G. et al. (1998). Breast-feeding during treatment with cyclosporine. Transplantation, 65 (2), 253-5. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/9458024

- Concentrations of cyclosporine in whole blood and breast milk were measured in seven kidney transplant and two kidney-pancreas patients and their breast-fed infants. Mother trough cyclosporine concentrations ranged from 55 to 130 ng/mL. Breast milk cyclosporine concentrations ranged from 64 to 227 ng/mL, samples were collected at random intervals. In all of the infants tested, none had whole blood cyclosporine levels that exceeded the lower limit of detection (30 mcg/mL). Serial cyclosporine measurements in breastmilk obtained for two patients illustrated concentration variation throughout the day.

14.3 Outcomes

Kaatz R, et al (2023). Pregnancy after Kidney Transplantation-Impact of Functional Renal Reserve, Slope of eGFR before Pregnancy, and Intensity of Immunosuppression on Kidney Function and Maternal Health. *J Clin Med*. 12(4):1545. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36836080/

- In a single-center study, risk factors contributing to adverse pregnancy outcomes were retrospectively analyzed in 40 women with post-transplant pregnancies after single or combined pancreas-kidney transplantation. 18 women experienced preeclampsia with severe end-organ dysfunction. Notably, impaired hyperfiltration during pregnancy was found to be a significant risk contributor for both adverse pregnancy events ($p < 0.05$) and deterioration of kidney function ($p < 0.01$). Investigators concluded that post-kidney transplant pregnancies showed good allograft and maternal outcomes.

van Buren MC, et al (2022). Effect of Pregnancy on eGFR After Kidney Transplantation: A National Cohort Study. *Transplantation*.106(6):1262-1270. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34456267/

- Nationwide multicenter cohort study in kidney transplant recipients (KTRs) with pregnancy (>20 wk) after kidney transplantation. There was a small, but insignificant, effect on eGFR slope in the first pregnancy, and the overall mean eGFR after the first, second, and third pregnancies was not significantly worse than pre-pregnancy eGFR ($p = 0.28$). There was an association between midterm hyperfiltration and better eGFR, as well as death-censored graft survival. This study concluded there was no significant effect of pregnancy on kidney function.

Chung K, et al. (2023). Emergent prelabor cesarean delivery in solid organ transplant recipients: associated risk factors and outcomes. Am J Obstet Gynecol MFM. 5(2):100799. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36368514/

- ∉ Retrospective cohort study of 1979 kidney and liver transplant recipients at >20 weeks gestation that aimed to characterize risk factors and outcomes of emergency prelabor cesarean delivery. The most frequent indication for emergent delivery was nonreassuring fetal heart tracing (86%). There was no significant difference in severe maternal morbidity in patients who underwent emergent prelabor cesarean delivery, but a significant increase in neonatal composite morbidity. Patients undergoing emergent delivery were less likely to deliver at a transplant center and more likely to have chronic hypertension.

Bedin A, et al. (2022). Pregnancies and gynecological follow-up after solid organ transplantation: experiences of a decade. J Clin Med. 11:4792. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36013030/

- Retrospective study of two French centers for kidney and lung transplantation. Most of the pregnancies were planned with an immunosuppressant switch from mycophenolate to azathioprine. Almost 64% of pregnancies resulted in live births with 21% miscarriages. The live births had a high incidence of preeclampsia (50%).

Meinderts J, et al. (2022). Follow-up of offspring born to parents with a solid organ transplantation: a systematic review. Transplant Int. 35:10565. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35992748/

- This article is a systematic review focused on greater than one year outcomes of children born to solid organ transplant recipient parents. Currently published results seem reassuring in terms of neurobehavioral, developmental, and immune function. These children do well compared to their peers and more studies are needed to assess long term outcomes.

Boyle S, et al. (2021). Pregnancy following heart transplantation: A single centre case series and review of the literature. Heart Lung Circ. 30(1), 144-153. Retrieved from: https://www.heartlungcirc.org/article/S1443-9506(20)31446-3/fulltext

- Case series of 3 women who became pregnant after heart transplantation. Patients were frequently monitored for cardiac function, tacrolimus levels, renal function, and common complications of pregnancy. There were no maternal or fetal deaths, no evidence of graft rejection, pre-eclampsia or deterioration in cardiac function. Gestational diabetes (n=3), cholestasis (n=1), and postpartum hemorrhage (n=1) occurred. The authors concluded that favorable pregnancy outcomes are achievable with preconception counseling, immunosuppression tailoring, and regular monitoring to avoid rejection and teratogenic complications.

Tang J, et al. (2021). Pregnancy outcomes for simultaneous Pancreas–Kidney transplant recipients versus kidney transplant recipients. Clin Transplant, 35(1), e14151. Retrieved from: https://onlinelibrary-wiley-com.ezproxymcp.flo.org/doi/epdf/10.1111/ctr.14151

- Retrospective review of 19 pregnancies in 15 simultaneous pancreas-kidney transplant recipients (SPKR) and 348 pregnancies in 235 kidney transplant recipients (KTR). Maternal ages, pre- and post-pregnancy creatinine, live birth rates, outcomes in type 1 diabetes or type 2 diabetes were similar in both groups. Additionally, maternal, fetal, and kidney transplant outcomes were also similar. However, the SPKR group had a shorter transplant to first pregnancy interval. The authors concluded that SPKR and KTR mothers have similar pregnancy outcomes.

Romano DN, et al. (2021). Orthotopic liver transplant in the pregnant recipient: A systematic review of preoperative management and maternal and fetal outcomes. Clin Transplant, e14269. Retrieved from: https://onlinelibrary.wiley.com/doi/10.1111/ctr.14269

- Systematic review of 22 patients who underwent liver transplantation during pregnancy. The article discussed causes of liver failure in these patients such as fulminant viral hepatitis (27%), drug-induced fulminant hepatic failure (14%), autoimmune hepatitis (9%), sickle cell disease (5%), decompensated biliary cirrhosis (5%), Budd-Chiari Syndrome (4%), and idiopathic (36%). The author discussed some of the preoperative, intraoperative, and postoperative management and clinical outcomes of these patients and their fetuses.

Valentin N, et al. (2021). Pregnancy outcomes after liver transplantation: A systematic review and meta-analysis. Am J Gastroenterol. 116(3), 491-504. Retrieved from: https://journals.lww.com/ajg/fulltext/2021/03000/pregnancy_outcomes_after_liver_transplantation__a.16.aspx

- Systematic review and meta-analysis evaluating pregnancy outcomes after liver transplantation (LT). The author discussed the impact of the interval from LT to pregnancy and immunosuppression on outcomes such as rates of live birth, preterm birth, and miscarriages. The rate of miscarriages was similar to the general population, however rates of preterm birth (32.1%) and preeclampsia (12.5%) were higher among LT recipients. The author concluded that pregnancy after LT is feasible but it does carry an increased risk of both maternal and fetal complications.

Sobotka LA, et al. (2021). Pregnancy in liver transplantation recipients is associated with increased complications and healthcare utilization. Am J Gastroenterol. 116(30), 560-567. Retrieved from:

https://oce.ovid.com/article/00000434-202103000-00024/HTML

- A retrospective chart review of pregnancy related admissions in liver transplant recipients. When compared to the general population, liver transplant recipients were more likely to undergo a caesarean delivery and have a pregnancy-related complication including miscarriage, intrauterine growth restriction, postpartum hemorrhage, hypertension, preeclampsia, thromboembolism, and longer hospital stay. However, the mortality rate during pregnancy in liver transplant recipients was zero compared with 4,784 (0.01%) in the general population. The author concluded that further research is needed to improve outcomes in this patient population.

Acuna S, et al. (2020). Pregnancy outcomes in women with cardiothoracic transplants: A Systematic review and meta-analysis. J Heart Lung Transplant, 39(2), 93-102. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31839511/

- Systematic review and meta-analysis of 385 pregnancies in 272 thoracic transplant recipients reporting the following complications: mortality during pregnancy, mortality during follow up, graft rejection, hypertensive disorders of pregnancy, and cesarean deliveries. Although 78.4% of the pregnancies resulted in live births, 51.2% were born preterm and neonatal deaths occurred in 3.4%. Congenital anomalies affected 4.3% of the newborns.

Boyer, A, et al. (2020). Paternity in male kidney transplant recipients: a French national survey, the PATeRNAL study. BMC Nephrol, 21(1), 483. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33198659/

- National French survey (self-reports) to assess rate of paternity among men (n = 232) who had received a kidney transplant and are using immunosuppressive medication(s). Specifically, though the immunosuppressants mycophenolate mofetil/mycophenolic acid (MMF/MPA) have been implicated in fetal malformations, researchers in this study found no warning signs of more pregnancy complications in the men studied compared to the general population.

Coscia L, et al. (2020). Pregnancy outcomes in 1164 female kidney transplant recipients. Transplantation, 104(S3), S573. Retrieved from: https://insights.ovid.com/obstetrics-gynecology/obsgy/2017/05/001/pregnancy-outcomes-following-cardiac-transplant/244/00006250

- Descriptive study of 2102 pregnancies from 1164 persons who had received a kidney transplant, identified from the Transplant Pregnancy Registry International 1991-2019. Researchers analyze data on immunosuppression medication use during pregnancy, pregnancy outcomes, and live birth outcomes. Researchers found live birth rate was 75% and organ rejection rate was 3%.

Coscia L, et al. (2020). Pregnancy outcomes in 331 female liver transplant recipients. Transplantation,104(S3), S42-S43. Retrieved from: https://journals.lww.com/transplantjournal/Citation/2020/09003/PREGNANCY_OUTCOMES_IN331_FEMALE_LIVER_TRANSPLANT.55.aspx

- Descriptive study of 651 pregnancies from 331 persons who had received a liver transplant, identified from the Transplant Pregnancy Registry International 1991-2019. Data includes immunosuppression medication use during pregnancy, pregnancy outcomes, and live birth outcomes. Researchers found live birth rate was 71% and organ rejection rate was 4.8%.

Kim JY, et al. (2020). Outcomes of living-donor kidney transplantation in female recipients with possible pregnancy-related pre-sensitization according to donor relationship. Ann Transplant, 25, e925229. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33154345/

- Retrospective review assessing the association between donor relatedness (i.e., offspring, husband, unrelated) and graft survival among living-donor kidney transplant recipients with a history of pregnancy. Offspring to mother had the lowest number of HLA mismatches, and husband to wife had the highest number of ABO-incompatible transplantations. At 5 years after transplant, graft survival, death-censored graft survival, and BPAR-free survival did not differ among the 3 groups.

Punnoose LR. et al. (2020). Pregnancy outcomes in heart transplant recipients. J Heart Lung Transplant, 39(5), 473-480. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32201090/

- Analysis of 91 heart transplant patients with 157 pregnancies. Average transplant to conception interval was 7 ± 6.1 years. Twenty percent of recipients continued mycophenolic acid while pregnant. Complications during pregnancy included preeclampsia and infections. Livebirths occurred in 69%. Miscarriages occurred in 26% of pregnancies, 49% of which had mycophenolic acid exposure.

van Buren MC, et al. (2020). Long-term graft survival and graft function following pregnancy in kidney transplant recipients: A systematic review and meta-analysis." Transplantation, 104(8), 1675-1685. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32732847/

- Meta-analysis and systematic review on graft loss and graft function, measured by serum creatinine after pregnancy in kidney transplant recipients, stratified in years postpartum revealed that mainly prepregnancy proteinuria, hypertension, and high serum creatinine are risk factors for graft loss. Pregnancy after kidney transplant has no effect on long-term graft survival and only a possible effect on graft function within 2 years postpartum.

Bachmann F, et al. (2019). Pregnancy following kidney transplantation - impact on mother and graft function and focus on childrens' longitudinal development. BMC Pregnancy & Childbirth, 19(1), 376. Retrieved from: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-019-2496-z

- Analysis of the impact of pregnancy on obstetrical risks, graft function, and fetal development of 32 pregnancies in 28 patients. Although there was a high rate of preterm birth and low birth weight, development up to two years was age-appropriate in this cohort.

Dumortier J, et al. (2019). Pregnancy and donor-specific HLA-antibody-mediated rejection after liver transplantation: “Liaisons dangereuses”? Transplant Immunology, 54, 47-51. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30743001/

- Single center, retrospective study of 73 female liver transplant patients of childbearing age to assess the impact of pregnancy on the occurrence and impact of DSA. Multivariate analysis disclosed that history of and younger age at liver transplantation were significantly associated with de novo DSA. The results suggest that close monitoring of DSA in young women with history of pregnancy should be recommended regarding the risk of DSA-mediated rejection.

Kamarajah SK, et al. (2019). Outcomes of pregnancy in recipients of liver transplants.Clin Gastroenterol Hepatol, 17(7), 1398-1404, e1391. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30529735/

- Assessment of morbidities and outcomes of 139 pregnancies in 83 women. Sixty-nine percent resulted in live births, 19% resulted in miscarriages or still births, and 9% were terminated. A higher proportion of patients who conceived more than 1 year after liver transplantation had live births than of women who conceived before this time. Tacrolimus exposure was associated with higher risks of premature delivery and caesarian section than cyclosporine exposure.

Kosoku A, et al. (2019). Successful pregnancy after in vitro fertilization in an ABO-incompatible kidney transplant recipient receiving rituximab: a case report. BMC Nephrol, 20(1), 206. Retrieved from: https://bmcnephrol.biomedcentral.com/articles/10.1186/s12882-019-1396-9

- Case report of a 35-year-old female kidney transplant recipient underwent an ABO-incompatible living-donor kidney transplant using rituximab. Two years after transplant, CD19(+) cells and CD20(+) cells remained depleted. Patient successfully gave birth to 2220 g girl by cesarean section. There were no complications during the perinatal period. Five years after transplant, the recipient has had no major complications including rejection or infection.

Prodromidou A, et al. (2019). Pregnancy outcomes after liver transplantation: A systematic review. Transplant Proc, 51(2), 446-449. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30879563/

- Systematic review through 2017 to assess the outcomes of pregnancy in patients with liver transplantation. Nineteen studies were included, which comprised 1290 pregnancies in 885 female recipients. Approximately one-third of pregnancies resulted in preterm birth. Spontaneous

abortions were reported in 176 cases and preeclampsia occurred in 188 patients.

Rajapreyar IN, et al. (2019). Management of reproductive health after cardiac transplantation. The Journal of Maternal-Fetal & Neonatal Medicine, 34(9), 1469-1478. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31238747/

- Review of reproductive health post cardiac transplant including a multidisciplinary approach and checklist to guide management.

DeFilippis E, Haythe J, Farr MA, Kobashigawa J, Kittleson MM. Practice patterns surrounding pregnancy after heart transplant. Circulation: Heart Failure. 13, e006811. Retrieved from: https://www.ahajournals.org/doi/10.1161/CIRCHEARTFAILURE.119.006811

- Analysis of 122 responses of a web-based survey sent to heart transplant providers. Thirty-one percent of respondents indicated that pregnancy should be avoided in all heart transplant recipients, and only 43% reported that their center had a formal policy regarding pregnancy following heart transplant.

Rao NN, et al. (2019). Successful pregnancy in a recipient of an ABO-incompatible renal allograft. Obstet Med, 12(1), 42-44. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30891092/

- Case report of a successful pregnancy in a renal transplant patient who underwent desensitization with rituximab and plasma exchange to receive an ABO-incompatible transplant two years prior to pregnancy. This recipient also had gestational diabetes, worsening renal function, and preterm delivery which are important complications often seen in pregnancies of solid organ transplant recipients.

Schreiber-Zamora J, et al. (2019). Evaluation of the body mass index (BMI) in children born to organ transplant recipients. J Matern Fetal Neonatal Med, 32(15), 2512-2516. Retrieved from: https://www.tandfonline.com/doi/full/10.1080/14767058.2018.1439468

- A comparison of BMI measurements performed in 61 children of transplanted women and 64 children born to healthy mothers revealed that obesity among children of mothers after kidney or liver transplants is more frequently observed.

Schreiber-Zamora J, et al. (2019). Neurological development of children born to mothers after kidney transplantation. J Matern Fetal Neonatal Med, 32(9), 1523-1527. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29157047/

- A comparison of neurological examinations performed in 36 children of kidney transplant women and 36 children born to healthy mothers revealed neurological development of children of kidney transplant women is similar to that of the general population and possible deviations seem to be the result of intrauterine hypotrophy and prematurity.

Shah S, et al. (2019). Pregnancy outcomes in women with kidney transplant: Metaanalysis and systematic review. BMC Nephrol, 20(1), 24. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6345071/

- Systematic review of studies reporting pregnancy with kidney transplant. Eighty-seven studies included, representing 6712 pregnancies in 4174 kidney transplant recipients. The authors concluded the outcome of live births is favorable, but the risks of maternal and fetal complications should be considered and counseled on in kidney transplant recipients.

Tebet JLS, et al. (2019). Pregnancy in renal transplant patients: Renal function markers and maternal–fetal outcomes. Pregnancy Hypertension, 15, 108-113. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30825905/

- Cross-sectional prospective study measuring renal function parameters and maternal and fetal data in 43 patients who became pregnant after renal transplantation. A gradual increase was observed in the following parameters during pregnancy and puerperium: serum creatinine levels, proteinuria, urinary protein/creatinine ratio, and albumin/creatinine ratio. Preeclampsia was the main cause of renal function decline at the end of pregnancy. Approximately 10% pregnant women presented with premature rupture of membranes and 42% with a urinary tract infection.

Combs J. et al. (2018). Belatacept during pregnancy in renal transplant recipients: Two case reports. American Journal of Transplantation, 18 (8), 2079-2082. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/29719109

- Case report on two renal transplant recipients who remained on belatacept during their pregnancy. Discusses lab variations and long-term outcomes of both women peri- and post-partum.

King RW. et al. (2017). Pregnancy outcomes related to mycophenolate exposure in female kidney transplant recipients. American Journal of Transplantation, 17 (1), 151-160. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/27321569

- Retrospective cohort study evaluating graft outcomes among kidney transplant recipients who became pregnant while on mycophenolate using The National Transplantation Pregnancy Registry data (n=382). Outcomes evaluated included miscarriages, birth defects and 2 and 5-year postpartum graft loss. The authors report no difference comparing those who discontinued mycophenolate >6 week prior to pregnancy and those who did not. Discontinuing mycophenolate during the second trimester or later increased risk of miscarriages (OR 9.35, 95%CI 4.31-20, p<0.001) and birth defects (OR 6.06, 95%CI 1.96-18.87, p = 0.002). Discontinuing mycophenolate <6 weeks prior to pregnancy increased risk of graft loss at 5 years compared to those who discontinued mycophenolate >6 weeks prior to pregnancy (OR 5.56, 95%CI 1.38-22.22, p=0.016).

King RW. et al. (2017). Discontinuing mycophenolate with respect to pregnancy and the interpretation of voluntary registry results. American Journal of Transplantation, 17 (2), 583-584. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Discontinuing+Mycophenolate+With+Respect+to+Pregnancy+and+the+Interpretation+of+Voluntary+Registry+Results

- King et al.'s response to the critique of their study. Importantly they acknowledge the risk of mycophenolate exposure in the first trimester is understated. They assert the original conclusion supporting FDA guidance to stop mycophenolate >6 weeks prior to conception is the best practice supported by their evidence.

Matilla M. et al. (2017). Pregnancy outcomes after liver transplantation in Finland. Acta Obstet Gynecol Scand, 96(9). Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/28574590

- Review of outcomes at liver transplant centers in Finland which resulted in good perinatal outcome with healthy, mostly full-term, normally grown offspring; however, serious maternal complications related to underlying liver pathology, transplant surgery and immunosuppressive medication occur frequently

Mohammadi FA. et al. (2017). Pregnancy outcomes and impact of pregnancy on graft function in women after kidney transplantation. Clinical Transplantation, 31 (10), e13089. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/28805261

- Retrospective study assessing graft outcomes from pregnancies occurring in a single center from 1976-2015. A total of 56 pregnancies in 35 women were reported. Live birth rate was 78.9%. Complications included hypertension (76%) and preeclampsia (30%). A third of the patients experienced graft function deterioration during pregnancy, of whom 63.2% did not recover to baseline.

Moritz MJ. et al. (2017). Mycophenolate and pregnancy: teratology principles and National Transplantation Pregnancy Registry experience. American Journal of Transplantation, 17 (2), 581-582. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Mycophenolate+and+Pregnancy%3A+Teratology+Principles+and+National+Transplantation+Pregnancy+Registry+Experience

- Investigators of the National Transplantation Pregnancy Registry letter to the editor responding to King et al.'s article above. The authors argue taking mycophenolate during the first semester of pregnancy increases risk of miscarriage and phenotypic birth defects. They identify their differing conclusion is a result of inappropriate patient and outcome grouping in the analysis.

Bhagra CJ. et al. (2016). Pregnancy in cardiac transplant recipients. Clinical Transplantation, 30 (9), 1059-65. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/27313061

- Single center retrospective study of all cardiac transplant patients who conceived from 1986 to 2014 (22 pregnancies in 17 women). Average time from transplant to conceive was 98 ± 62.4 months. Rejection occurred in one pregnancy which was attributed to noncompliance with immune suppression, LV function was unchanged in all other cases. Complications included hypertension (13.6%), preeclampsia (13.6%), and cholestasis (4.5%). Twenty pregnancies, 11 of which were caesarean section, resulted in live births, and 4 infants required special neonatal cares. Since pregnancy, four women have died, one from postpartum hemorrhage, two from non-compliance and one of graft coronary disease.

Jabiry-Zieniewicz Z. et al. (2016). Pregnancy in the liver transplant recipient. Liver Transplantation, 22 (10), 1408-17. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/27197796

- Review of recent literature and single center experience of pregnancy following liver transplantation. The authors provide management recommendations for each phase of the liver transplant recipients pregnancy journey, from pregnancy prevention to breast feeding.

Morken NH. et al. (2015). Obstetric and neonatal outcome of pregnancies fathered by males on immunosuppression after solid organ transplantation. American Journal Transplantation, 15 (6), 1666-73. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/25868657

- National population-based retrospective cohort study including male transplant recipients from 1967-2009. Data retrieved from the Medical Birth Registry of Norway. A total of 474 babies were identified as having fathers who were transplant recipients and 4614 babies who were fathered by males before undergoing transplantation. Compared to the general population, paternal solid organ transplant deliveries did not differ in rates of major malformations or preterm delivery. An observed increased risk in preeclampsia and small-forgestational-age was found (50% and 30%, respectively) in the paternal solid organ transplant deliveries compared to the general population, not statistically significant. Rates of preeclampsia were increased in the paternal solid organ transplant deliveries compared to the general population (adjusted odds ratio 1.5, 95%CI 1.0-2.3). This increased rate in preeclampsia held true comparing pregnancies fathered prior to transplantation and after (adjusted odds ratio 7.4, 95%CI 1.1-51.4), though this difference was not statistically significant once patients identified as having a child with more than one partner were excluded.

Coscia LA. et al. (2014). Immunosuppressive drugs and fetal outcome. Best Practice and Research Clinical Obstetrics and Gynaecology, 28 (8), 1174-87. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/25175414

- Literature review and evaluation of National Transplantation Pregnancy Registry data relating to immunosuppressive agents used in pregnancy.

Hebral AL. et al. (2014). Pregnancy after kidney transplantation: outcome and antihuman leucocyte antigen alloimmunization risk. Nephrology Dialysis and Transplantation, 29 (9), 1786-93. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/24914091

- Single center retrospective study from 1969-2011 including 46 female solid organ transplant recipients and 61 pregnancies, 89% of which were planned and 93% resulted in live births. Complications during pregnancy included preeclampsia (26%), gestational diabetes (21%), infection (23%), threat of premature delivery (16%), intrauterine growth retardation (15%), haemorrhage at delivery (7%). Gestational diabetes occurred more frequently in patients receiving tacrolimus compared to cyclosporine (35% vs 7.7%, p=0.02). Renal function was stable during pregnancy and post delivery. Neonates with low birth weights occurred in 15% of cases and three malformations were diagnosed. Immunologic profiles were assessed before and after pregnancy. De novo donor specific antibodies were detected in three transplant recipients (5.9%). The authors note that in 2 of the 3 cases of donor specific antibody development the child's father shared HLA subtype with the deceased organ donor.

Jones A. et al. (2013). Outcomes of pregnancies fathered by solid-organ transplant recipients exposed to mycophenolic acid products. Progress in Transplantation, 23 (2), 153-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/23782663

- Observational cohort of 152 solid organ transplant recipients who fathered 205 pregnancies while taking mycophenolate. Data was gathered from the National Transplantation Registry. Of the 194 live births reports, only 6 resulted in fetal malformations (3.1%), similar to the general population.

Wyld ML. et al. (2013). Pregnancy outcomes for kidney transplant recipients. American Journal of Transplantation, 13 (12), 3173-82. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/24266970

- This study reviewed 692 pregnancies to 447 kidney transplant recipients between 1971 and 2010. The data highlights that the overall outcomes for babies of women with transplants have improved over the past 40 years, contrary to past research which has shown that babies born to transplant recipients are more likely to be born preterm. This analysis demonstrated that the only factor impacting gestational age that remains is the length of time between transplantation and pregnancy.

Deshpande NA. et al. (2012). Pregnancy outcomes of liver transplant recipients: a systematic review and meta-analysis. Liver Transplantation, 18 (6), 621-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/22344967

- Systematic review and meta-analysis of literature reporting pregnancy outcomes in liver transplant recipients from 2000-2011. Of the 578 studies identified, 50 pregnancies are reported in 306 liver transplant recipients. The authors report a live birth rate of 76% (95%CI 72.7-80.7%), miscarriage rate of 15.6% (95%CI 12.3-19.2%), preeclampsia rate of 21.9% (95%CI 17.7-26.4%), cesarean section rate of 44.6% (95%CI 39.2-50.1%), and preterm delivery rate of 39.4% (95%CI 33.1-46%).

Perales-Puchalt A. et al. (2012). Pregnancy outcomes after kidney transplantation immunosuppressive therapy comparison. Journal of Maternal-Fetal and Neonatal Medicine, 25 (8), 1363-6. Retrieved from:

https://www.ncbi.nlm.nih.gov/pubmed/?term=Pregnancy+outcomes+after+kidney+tra nsplantation-immunosuppressive

- Single center retrospective study evaluating pregnancies occurring post transplantation from 1995-2009 in 23 patients. Of 29 pregnancies, 26 resulted in live births. Immunosuppressive medications included cyclosporine (n=11), tacrolimus (n=9), mycophenolate (n=1), and azathioprine (n=12). One infant suffered a cleft palate malformation; the mother was immunosuppressed with mycophenolate. No significant change in maternal renal function was observed from before pregnancy to post delivery.

Shaner J. et al. (2012). Pregnancy after lung transplant. Progress in Transplantation, 22 (2), 134-40. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Pregnancy+after+lung+transplant+shan er

- Retrospective cohort study using data from the National Transplantation Pregnancy Registry to evaluate pregnancy outcomes in lung transplant recipients. Twenty-one lung female transplant recipients were included, reporting 30 pregnancies. Lung transplant patients had a higher rate of premature birth compared to other transplant populations but the author did not concluded there was any difference in long term outcomes between the children.

Celik G. et al. (2011). Biochemical parameters, renal function, and outcome of pregnancy in kidney transplant recipient. Transplant Proceedings, 43 (7), 2579-83. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/21911126

- This retrospective study investigated the effects of pregnancy on long-term renal function as well as the prognosis of pregnancy and delivery among renal transplant recipients. The study highlights significant differences between creatinine, bicarbonate, albumin, triglycerides and proteinuria levels according to preconception, gestational, and postpartum sampling.

Deshpande NA. et al. (2011). Pregnancy outcomes in kidney transplant recipients: a systematic review and meta-analysis. American Journal of Transplantation, 11 (11), 2388-404. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/21794084

- This review highlights studies of pregnancy-related outcomes in kidney transplant recipients. Fifty articles were included in this analysis, representing 4706 pregnancies in 3570 kidney transplant recipients. Hypertension, elevated serum creatinine and proteinuria are described in association with adverse pregnancy outcomes.

Veroux M. et al. (2011). Pregnancy under everolimus-based immunosuppression. Transplantation International, 24 (12), e115-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/21950359

- Case report of a 30 year old female with a history of acute rejection, immune suppressed with everolimus, cyclosporine and prednisone, who presented 12 weeks pregnant. She continued on the same immune suppression for the remainder of the pregnancy. The patient delivered by cesarean section during week 30, after the mother presented with worsening renal function and proteinuria and severe hypertension. The child was born without malformation and the mother's renal function improved by the 6 months postpartum follow visit.

Coscia LA. et al. (2010). Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. Clinical Transplantation, 65-85. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/21698831

- National Transplantation Pregnancy Registry report on outcomes from 2,000 pregnancies post transplantation.

Gill JS. et al. (2009). The pregnancy rate and live birth rate in kidney transplant recipients. American Journal of Transplantation, 9 (7), 1541-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/19459800

- Observational study of 16,195 female kidney transplant recipients from 1990 to 2003, age 15-45 years, using United States Renal Data System data. Pregnancy rate within 3 years of transplant was 33 per 1,000 females based on Medicare claims data. Live birth rate was 19 per 1,000 females. Pregnancies resulting in fetal loss remained constant at 45.6%. The authors compare the results reported to the National Transplantation Pregnancy Registry and UK Transplant Pregnancy Registry which use voluntary registries and report much higher live birth rates.

Kim HW. et al. (2008). The experience of pregnancy after renal transplantation: pregnancies even within postoperative 1 year may be tolerable. Transplantation, 85 (10), 1412-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Pregnancies+even+within+postoperative+1+year+may+be+tolerable.

- This is a retrospective analysis looking at graft, fetal, and maternal outcomes of pregnancy in renal transplant recipients.

Surti B. et al. (2008). Pregnancy and liver transplantation. Liver International, 28 (9), 1200-6. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Surti+Pregnancyand+liver+transplantati on

- Review of management of the pregnancy in liver transplant recipients and available literature.

Sibanda N. et al. (2007). Pregnancy after organ transplantation: a report from the UK Transplant Pregnancy Registry. Transplantation, 83 (10), 1301-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/17519778

- Outcomes reported from 193 kidney transplant recipients in the United Kingdom Transplant Pregnancy Registry. Notably 50% of pregnancies in renal transplant patients resulted in live births. The analysis suggested an association between hypertension during pregnancy and worse post pregnancy graft survival. Serum creatinine greater than 150 mol/L prior to pregnancy was associated with worse renal function after pregnancy.

Guardia O. et al. (2006). Pregnancy under sirolimus-based immunosuppression. Transplantation, 81 (4), 636. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/16495817

- Letter to the editor outlining a case report of a successful pregnancy of a renal transplant recipient while immunosuppressed with sirolimus, cyclosporine and prednisone.

Sifontis NM. et al. (2006). Pregnancy outcomes in solid organ transplant recipients with exposure to mycophenolate mofetil or sirolimus. Transplantation, 82 (12), 1698-702. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/17198262

- Study examining outcomes of pregnancies with exposure to mycophenolate or sirolimus using data from the National Transplantation Pregnancy Registry. Of the pregnancies exposed to

mycophenolate (n=26) there were 15 live births and 11 spontaneous abortions. Of the live births exposed to mycophenolate, 4 children had structural malformations (26.7%). Seven transplant recipients became pregnant while taking sirolimus resulting in 4 live births one of which had a structural abnormality. The authors noted the structural abnormality observed in the sirolimus group was from a mother who was switched from mycophenolate late during pregnancy.

McKay DB. et al. (2006). Pregnancy in recipients of solid organs-effects on mother and child. New England Journal of Medicine, 354 (12),1281-93. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/16554530

- Review article outlining the risk of pregnancy post transplantation on the mother and fetus. The authors used volunteer patient registries and available literature to describe the the frequency of complications in post transplant pregnancies including hypertension, preeclampsia, graft loss and rejection. The authors also review fetal exposure to immunosuppressive medications during gestation and then through breastmilk.

Fischer T. et al. (2005). Effect of pregnancy on long-term kidney function in renal transplant recipients treated with cyclosporine and with azathioprine. American Journal of Transplantation, 5 (11), 2732-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/16212634

- Retrospective cohort studying pregnancy in transplant data from five German transplant centers. Transplant recipients who conceived (n=81) were matched to a control group. Pregnant transplant recipients receiving azathioprine and prednisone were compared to those receiving cyclosporine and the matched control group. Outcomes of interest include graft survival, patient survival, and long term graft function with the authors observing no difference between the groups for any outcome studied.

Kainz A. et al. (2000). Review of the course and outcome of 100 pregnancies in 84 women treated with tacrolimus. Transplantation, 70 (12), 1718-21. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/11152103

- Retrospective analysis from 1992 to 1998 where case reports of tacrolimus use during pregnancy from clinical studies, reports from health care professionals and surveys of transplant registries were evaluated (100 pregnancies, 84 mothers). One patient included was taking tacrolimus for an autoimmune disorder, the remaining were solid organ transplant recipients. Of the 100 pregnancies studied, 71 progressed to delivery. Complications during pregnancy following transplantation include rejection (n=9), preeclampsia (n=8), renal impairment (n=7), and infection (n=6). All cases of rejection were treated with bolus steroids, no reports of graft loss. Four fetal malformations were reported.

Armenti VT. et al. (1995). Variables affecting birth weight and graft survival in 197 pregnancies in cyclosporine-treated female kidney transplant recipients. Transplantation, 59 (4), 476-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Variables+affecting+birthweight+and+graft+survival+in+197+pregnancies+in+cyclosporinehttps://www.ncbi.nlm.nih.gov/pubmed/?term=Variables+affecting+birthweight+and+graft+survival+in+197+pregnancies+in+cyclosporine-treated+female+kidney+transplant+recipientstreated+female+kidney+transplant+recipients

- Retrospective review of 141 transplant patients experiencing 197 pregnancies who were immunosuppressed with cyclosporine before and during pregnancy. Common complications included premature birth (54% delivered at less than 37 weeks), low birth weights (50% less than 2.5 kg), maternal hypertension (56%), preeclampsia (29%), infections (22%) and rejection (11%).

Murray JE. et al. (1963). Successful pregnancies after human renal transplantation. New England Journal of Medicine, 269, 341-3. Retrieved from: https://www.nejm.org/doi/full/10.1056/NEJM196308152690704

- This article begins with a case report on a successful living kidney donation amongst identical twins. It chronicles the restoration of fertility and pregnancy of the recipient. Both individuals went on to deliver normal infants post donation and transplantation, respectively.

14.4 Living Donor Outcomes

Pippias M, et al. (2022). Pregnancy after living kidney donation, a systematic review of the available evidence, and a review of the current guidance. Am J Transplant. 22(10):2360-2380. Retrieved from https://pubmed.ncbi.nlm.nih.gov/35716049/

- Systematic review of 16 studies including 1,399 post kidney donation pregnancies, examining complications in post-donation pregnancies. These complications were compared to the risks of pregnancy-induced complications in women who have not undergone a donor nephrectomy. The authors also identified areas which could be addressed in guidelines and consensus statements focusing on pregnancy post kidney donation.

Fujita A, et al. (2021) Mothers' experiences with pregnancy and childbirth following pediatric living liver transplant donation: a qualitative descriptive study. Transplant Proc. 53(2), 630-635. Retrieved from: https://www.sciencedirect.com/science/article/pii/S004113452032889X

- This is a case report of 11 living liver donors who underwent pregnancy and childbirth after donor surgery. The author describes 6 categories of the mothers' experiences concluding that continuous emotional support for these mothers are paramount.

Kim JY, et al. (2020). Outcomes of living-donor kidney transplantation in female recipients with possible pregnancy-related pre-sensitization according to donor relationship." Ann Transplant, 25, e925229. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7653973/

- Researchers investigated pregnancy outcomes of female kidney transplant recipients from living donors (offspring, husband, or unrelated person). There was no statistical significance for the primary endpoints graft survival and biopsy proven rejection for recipient regardless of whether they had received a graft from an offspring, husband, or unrelated person. Recipients did not exhibit worse clinical outcomes after receiving a graft from an offspring, husband, or unrelated person

Davis S, et al. (2019). Risk of adverse maternal and fetal outcomes during pregnancy in living kidney donors: A matched cohort study. Clinical Transplantation, 33(1), e13453. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30472740/

- Case-control study where researchers investigated women (n = 59) who had donated a kidney before their first pregnancy matched to controls (similar age and race) identified from an integrated healthcare delivery system in the US. Women who had donated a kidney did not have higher adverse outcomes compared to matched controls. Researchers noted a trend towards increased risk of preeclampsia/eclampsia (Odds ratio [OR]: 2.96, 95% CI: 0.98-8.94, P = 0.06). They also noted a fourfold increased risk of preeclampsia/eclampsia in donors <30 years of age (OR: 4.09, 95% CI: 1.07-15.59, P = 0.04).

van Londen M, et al. (2018). Overweight young female kidney donors have low renal functional reserve postdonation. American Journal of Physiology - Renal Physiology, 315(3), F454-F459. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29357424/

- Retrospective study where researchers expanded on previous research findings: higher body mass index (BMI) was associated with low postdonation renal functional reserve (RFR) to look for a possible relationship between overweight BMI (> 25) and RFR of female donors (age < 45 years) pre/post donation. Study participants (n = 105) were overweight donors BMI of 25 (22-27) kg/m^2, with age 41 (36-44 median interquartile range). Researchers found a statistically

significant inverse, negative relationship between high BMI and adequate RFR, independent of confounders (standardized beta 0.37, P = 0.02). After organ donation, researchers noted wholly lost RFR (1 ml/min vs. 10 ml/min predonation, P < 0.001). Increased risk for end-stage kidney disease and preeclampsia may be associated with low RFR and warrants further investigation in research such as prospective studies.

Garg AX. et al. (2014). Gestational hypertension and preeclampsia in living kidney donors. New England Journal of Medicine, 372 (2), 124-33. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4362716/

- Retrospective cohort of 85 living kidney donor outcomes after 131 pregnancies following kidney donation. Study subjects were matched with non-donors from the general population. Gestational hypertension was more common in kidney donors (odds ratio 2.4, 95%CI 1.2-5; p=0.01). Preeclampsia was also more common among kidney donors.

Ibrahim HN. et al. (2009). Pregnancy outcomes after kidney donation. American Journal of Transplantation, 9 (4), 825-34. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/19353771

- This survey of previous living donors evaluated fetal and maternal outcomes as well as pregnancy outcomes after kidney donation and found similar outcomes to those reported in the general population, but inferior to pre-donation pregnancy outcomes.

Nevis IF. et al. (2009). Maternal and fetal outcomes after living kidney donation. American Journal of Transplantation, 9 (4), 661-8. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/19344459

- Review of literature regarding pregnancy outcomes in women post kidney donation. Outcomes of gestational hypertension, preeclampsia, premature birth and low birth weights were collected for the general population and in women post kidney donation for comparison. Though individual studies report slight increases incidence of gestational hypertension and preeclampsia, after reviewing the literature available, the authors conclude that kidney donation does not pose great harm to pregnancy, rather the donor should be monitored more closely during pregnancy.

Soyama A. et al. (2007). Pregnancy and delivery after partial liver donation for living donor liver transplantation. Transplantation, 84 (2), 283. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/17667826

- Case report describing the pregnancy of a living liver donor within 6 months of donation. The pregnancy proceeded to deliver without complication.

14.5 Contraception

McIntosh T, et al. (2023). A survey of solid organ transplant recipient attitudes and concerns regarding contraception and pregnancy. Clin Transplant. Epub ahead of print. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36822220/

- Survey of 243 female SOT recipients of childbearing age to understand patient attitudes regarding post-transplant contraception preferences and pregnancy concerns. Only 4.5% of recipients who were not using contraception did not think SOT recipients could become pregnant. Less than 50% of respondents remembered signing the mycophenolate REMS document. Fetal and maternal health complications were the most common pregnancy concerns among respondents.

Lew J, et al. (2021). Etonogestrel contraceptive implant uptake and safety among solid organ transplant recipients. Contraception. 104: 556-560. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34147509/

- Retrospective cohort study that matched women of reproductive age who used etonogestrel implants with those who didn't. Contraceptive implants did not correlate with an increased risk for adverse transplant outcomes. No difference in pregnancy, infection and immunosuppression outcomes was found. This is the first study to show that etonogestrel implants are safe to use for contraception in solid organ transplant recipients of reproductive age.

Klein CL, et al. (2021). Post-transplant Pregnancy and Contraception. Clin J Am Soc Nephrol. CJN.14100820. Retrieved from: https://cjasn.asnjournals.org/content/clinjasn/early/2021/03/16/CJN.14100820.full.pdf?with-ds=yes

- Review article discussing options for contraception, importance of reproductive counseling, immunosuppression considerations, and pregnancy risks to the allograft. The author concluded that pregnancy after kidney transplant can occur safely when planned carefully with modifications to immunosuppression.

Davis-Kankanamge C, et al. (2020). Menstruation and contraception patterns of female adolescent transplant recipients. Pediatr Transplant, 24(7), e13817. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32808738/

- Cross-sectional descriptive survey of 19 adolescent female transplant patients on mycophenolate mofetil from April 2016 through May 2017. The average age of the patient was 16.2 years. The type of transplants includes renal (57.1%), heart (23.8%), and liver (4.8%). Reported menstrual concerns included dysmenorrhea, irregular bleeding, and heavy bleeding pre- and post-transplant, respectively. Participants reported contraceptive counseling prior to and after transplant approximately half of the time.

Eide IA, et al. (2019). Contraceptive choices and counseling in Norwegian female renal transplant recipients. Transplant Proc, 51(2):470-474. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30879570/

- Norwegian multicenter retrospective observational study of 118 female renal transplant recipients 22-49 years old. Patients were given a questionnaire on fertility, contraceptive use, and pregnancy. Thirty seven percent of patients reported that they did not receive advice on contraceptive methods from health care personnel in the early post-transplant phase Forty-five percent reported that they had not received any advice on timing of conception after transplant.

Gordon C, et al. (2019). Controversies in family planning: intrauterine device placement in solid organ transplant patients. Contraception, 100(3), 250-252.Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31153820/

- Case report and review of the literature regarding IUD use in transplant patients.

Maroo A, Chahine J (2018). Contraceptive strategies in women with heart failure or with cardiac transplantation. Curr Heart Fail Rep. 2018 Jun;15(3):161-170. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/29616492

- Review of literature in cardiac transplant specific contraception, stratifying by complicated post-operative course and uncomplicated transplant course.

Rupley DM. et al. (2014). Preconception counseling, fertility, and pregnancy complications after abdominal organ transplantation: a survey and cohort study of 532 recipients. Clinical Transplantation, 28 (9), 937-45. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/24939245?dopt=Abstract

- This survey of abdominal transplant female patients discusses transplant-specific outcomes in both mother and fetus. It also illustrates survey responses regarding how patients were counseled about pregnancy after transplantation.

Szymusik I. et al. (2014). Contraception in women after organ transplantation. Transplant Proceedings, 46 (10), 3268-72. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/25498036

- This survey illustrates the need for improved family planning methods in female transplant recipients of reproductive age. It discusses the various contraceptive methods available to women, their specific relevance in the transplant population, as well as their prevalence of use in this population.

French VA. et al. (2013). Contraception and fertility awareness among women with solid organ transplants. Obstetrics Gynecology, 122 (4), 809-14. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5600476/

- Survey of 183 women post transplantation from a single center to investigate fertility awareness and quality of contraceptive counseling following transplant. Of the women surveyed, 44% did not know women could conceive following transplantation and only 36% reported a healthcare provider discussed the potential for pregnancy after transplantation. The authors also report the frequency and types of contraceptive use post transplantation.

Krajewski CM. et al. (2013). Contraceptive options for women with a history of solid organ transplantation. Transplantation, 95 (10), 1183-6. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/23358183

- Since restoration of fertility can return as soon as one month after transplantation, the Centers for Disease Control and Prevention (CDC) issued formal recommendations to guide contraceptive use in solid organ transplant recipients. This article reviews those recommendations including the benefits of long-acting reversible contraception specifically in the transplantation population.

Paulen ME. et al. (2010). Contraceptive use among solid organ transplant patients: a systematic review. Contraception, 82 (1), 102-12. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/20682148

- Systematic literature review using PubMed through 2009 to assess the contraceptive use among women having undergone solid organ transplantation. Eight articles from seven studies were included. The authors conclude that the data available indicated combined oral contraceptives and transdermal contraceptive patch effectively prevented pregnancy without significant variation in biochemical measures from the general population. Evidence to assess the other forms of contraception were not available.

Guazzelli CA. et al. (2008). Contraceptive counseling and use among 197 female kidney transplant recipients. Transplantation, 15; 86 (5), 669-72. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/18791448

- Single center study in which 197 women kidney transplant recipients of reproductive age were interviewed. Following transplant 50.2% of recipients reported menstrual irregularity compared to 70.6% prior; 79.7% of recipients were sexualy active compared to 91.9% prior; 48.7% were advised to use contraception compared to 74.1% prior; and 72.1% were using a contraception method compared to 86.3% prior. Among those interviewed there were 14 pregnancies after transplant, 92.9% of which were unplanned.

14.6 Pregnancy planning/fertility

Pollard AL, et al (2023). Supporting Reproductive Care for Patients Requiring Solid Organ Transplant. NWH. 27(1):53-64. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36567068/

- Review of the complex needs of patients after transplant and the need for thorough education about immunosuppressant medications, contraceptive methods, and expected waiting periods before conceiving. The article highlights actions nurses can take to provide effective, safe, comprehensive, and inclusive reproductive care to patients posttransplant.

Kittleson MM, et al (2023). Reproductive health after thoracic transplantation: An ISHLT expert consensus statement. J Heart Lung Transplant. 42(3):e1-e42. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36528467/

- Consensus statement from ISHLT summarizing the current evidence regarding pregnancy after thoracic transplantation. Guidance provided on preconception counseling, patient risk assessment, medical management, maternal and fetal outcomes, obstetric management, and pharmacologic considerations.

Castillo A, et al. (2022). Maternity after orthotopic liver transplantation: can the use of biological fertility indicators help? Our own experiences and literature-based recommendations. Linacre Q. 89:135-151. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35619884/

- Case report regarding the use of biological fertility technology and monitoring to not only prevent pregnancy but also safely induce one. Patient studied was a liver transplant recipient who desired more children after transplant and achieved a healthy delivery by this method.

Rahim MN, et al. (2021). Safety and efficacy of in vitro fertilisation in patients with chronic liver disease and liver transplantation recipients. J Hepatol, S0168-8278(21), 00005-2. Retrieved from:

https://www.journal-of-hepatology.eu/article/S0168-8278(21)00005-2/fulltext

- Retrospective review of 42 women with liver-related subfertility (LRSF). Approximately 75% of IVF cycles had successful implantation. There were few miscarriages and unsuccessful IVF attempts. Some notable complications included obstetric cholestasis, hypertensive disorder, and decompensated autoimmune hepatitis-related cirrhosis. However, the number of cases was small. Half of the pregnancies resulted in premature deliveries. The authors concluded that IVF in women with LRSF can be successful albeit increased risks of complications.

Ritchie J, et al. (2020). Family planning in liver transplant: Patient and provider knowledge and practices. Liver Transpl, 26(10), 1233-1240. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32583555/

- Cross-sectional study, survey of pre/post-transplant patients and providers to ascertain their knowledge on contraception and pregnancy; information collected included quantification of occurrence of reproductive counseling, priority of family planning as part of transplant care, type of counseling received, along with modalities used for of counseling; Researchers noted most patients received fertility counseling, but contraception practices were inadequate to prevent unplanned pregnancies. The most preferred modality by patients for reproductive counseling was face-to-face interaction with providers.

Szymusik I, et al. (2020). Infertility in female and male solid organ recipients - from diagnosis to treatment: An up-to-date review of the literature. Ann Transplant, 25, e923592. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7684845/

- Researchers highlight 20-30% of transplanted patients are in their reproductive years and have a slightly higher rate of infertility than the general population. There is information on specifics effects of transplant medications on reproduction. This information should be shared by healthcare providers with patients. Assisted reproductive techniques can be considered and offer favorable results for transplant patients in their reproductive years.

Pais AS, et al. (2019). Fertility preservation with successful pregnancy outcome in a patient with transplanted heart and non-Hodgkin's lymphoma - a case report. BMC Pregnancy & Childbirth, 19(1), 421. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31744460/

- Case report of a successful pregnancy outcome in a woman status post heart transplant and pelvic non-Hodgkins Lymphoma (iatrogenic ovarian failure after pelvic radiation) who had preserved oocytes and embryos.

Phillips, PK, Saha, S, Foley, DP, Iruretagoyena, JI, & Said, A. (2019). Deficiencies in reproductive health counseling in liver transplant recipients. Clin Transplant, 33(8), e13631. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31744460/

- Researchers reviewed documentation of counseling for male and female liver transplant recipients from one US center (1994-2015). Despite the quick return to fertility in this population there is a low (albeit rare) rate of documentation of reproductive health counseling.

Yaprak M, et al. (2019). In vitro fertilization after renal transplantation: A single-center experience. Transplant Proc, 51(4), 1089-1092. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31101177/

- Retrospective single center study included survey methodology to analyze the experience of patients (n= 13) receiving IVF. There is a favorable (25%) live-birth rate using IVF procedures.

Sarkar M. et al. (2018). Reproductive health in women following abdominal organ transplant. American Journal of Transplantation, 18 (5), 1068-1076. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Reproductive+health+in+women+following+abdominal+organ+transplant

- This article addresses a myriad of reproductive health topics and family planning recommendations following abdominal organ transplantation. Such topics include fertility in the pre- and posttransplant setting, contraception in transplant
- recipients, pregnancy outcomes in transplant recipients, immunosuppression risks with pregnancy, and breastfeeding after transplant.

Rose C. et al. (2016). Timing of pregnancy after kidney transplantation and risk of allograft failure. American Journal of Transplantation, 16 (8), 2360-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/26946063

- This observational study looked at the risk of allograft failure among 729 women who became pregnant within the first 3 posttransplant years. The probability of allograft failure from any cause including death (ACGL) increased with the number of years after pregnancy.

Zuber J. et al. (2008). Sirolimus may reduce fertility in male renal transplant recipients. American Journal of Transplantation, 8 (7), 1471-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/18510638

- Observational study of male kidney transplant recipients age 20-40 years between 1995-2005 (n=95). Patients were sent a questionnaire and a sperm analysis was performed for consenting participants (n=33). Male transplant recipients immune suppressed with sirolimus had a reduced sperm count compared to those not taking sirolimus (28.6 ± 31.2 * 10^6 and 292.2 ± 271.2 *

10^6, respectively, p=0.006). The proportion of motile spermatozoa was also decreased in transplant recipients taking sirolimus compared to those who were not (22.2 ± 12.3% and 41 ± 14.5%, respectively, p=0.01). Patients taking sirolimus containing immune suppression regimens fathered fewer pregnancies compared to those taking sirolimus-free regimens (5.9 95%CI 0.8-42 pregnancies/1,000 patient years compared to 92.9 95%CI 66.4-130 pregnancies/1,000 patient years, p=0.007).

Huyghe E. et al. (2007). Gonadal impact of target of rapamycin inhibitors (sirolimus and everolimus) in male patients: an overview. Transplant International, 20 (4), 305-11. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Gonadal+impact+of+target+of+rapamycin+inhibitors+(sirolimus+and+everolimus)+in+male+patients%3A+An+overview.

- Review evaluating the effect of mTOR inhibitors on testosterone, follicle stimulating hormone, luteinizing hormone, sexual function, fertility and sperm mobility. The authors conclude mTOR inhibitors decrease testosterone levels, increase luteinizing hormone levels and disrupt spermatogenesis.

Bererhi L. et al. (2003). Rapamycin-induced oligospermia. Transplantation, 76 (5), 8856. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Rapamycinhttps://www.ncbi.nlm.nih.gov/pubmed/?term=Rapamycin-induced+oligospermiainduced+oligospermia.

- Case report of a male kidney transplant recipient immune suppressed with prednisone and sirolimus who had a sperm analysis demonstrating impaired motility and altered structure. Sirolimus was changed to tacrolimus and he continued on prednisone for immunosuppression. After two months his sperm analysis returned to normal.

14.7 Complications

Yadav A, et al. (2022). Acute kidney injury during pregnancy in kidney transplant recipients. Clin Transplant. 36(5):e14668. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35396888/

- Review article assessing causes and outcomes of pregnancy-related AKI in the kidney transplant population. Authors further discuss management strategies pregnancy-related AKI in this patient population.

Yin O, et al. (2021). Differentiating Acute Rejection From Preeclampsia After Kidney Transplantation. Obstet Gynecol. 137(6):1023-1031. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33957644/

- Retrospective case-controlled registry study evaluating clinical and laboratory characteristics in pregnancy that differentiate preeclampsia from acute renal allograft rejection. Investigators also assessed maternal, neonatal, and graft outcomes of these diagnoses. Data was abstracted from Transplant Pregnancy Registry International deliveries between 1968 and 2019.

Balaha M, et al. (2019). Thymoglobulin-resistant T-cell-mediated rejection in a pregnant renal transplant recipient: Case report and review of the literature." Exp Clin Transplant, 17(Suppl 1), 159-163. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30777545/

- A female renal transplant recipient who became pregnant in about two years after her living-donor renal transplant. While pregnant, she presented with acute graft dysfunction with a serum creatinine of 4.13 mg/dL and received empiric pulse steroids and IVIG without response. Biopsy showed acute t-cell-mediated rejection and negative C4d. She received 5 doses (1 mg/kg/day) of thymoglobulin. She vaginally delivered a viable 2-kg boy.

Yoshikawa Y, et al. (2019). Childbirth and care difficulties of female kidney transplantation recipients. Transplant Proc, 51(5), 1415-1419. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31076146/

- Cross-sectional analysis of 65 Japanese kidney transplant recipients from 21 hospitals who had

given birth after transplant. Patients a questionnaire regarding childcare-related sufferings. Six categories identified the most common difficulties in childcare experience by mothers who gave birth after kidney transplant: comparing themselves with healthy mothers, parenting priorities, getting tired, not being able to take medicine on time, carefully giving the child a hug, being unable to give breast milk, having regular doctor checkups, and having to leave the child.

Zammarchi L, et al. (2020). Management of cytomegalovirus infection in pregnancy: is it time for valacyclovir? Clin Microbiol Infect, 26(9): 1151-1154. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32289479/

- Review of available data (one observational study, three clinical trials, two case reports) on the use of valacyclovir during pregnancy to prevent and treat CMV infection and disease. Clinical trials showed a decrease in both vertical transmission and an increase in asymptomatic neonates in patients treated with 8g/day valacyclovir compared to historical cohort of untreated pregnancies. Valacyclovir is considered 'off label' use for CMV in pregnancy.

Shah PB. et al. (2018). Preeclampsia risks in kidney donors and recipients. Current Hypertension Reports, 20 (7), 59. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/29884919

- Review of current literature evaluating preeclampsia risk in kidney transplant recipients and kidney donors. In addition to synthesizing the various preeclampsia rates from available sources, the authors evaluate risk factors for preeclampsia, the usefulness of risk calculators and strategies to minimize preeclampsia occurrence.

Kutzler HL. et al. (2016). Administration of antithymocyte globulin (rabbit) to treat a severe, mixed rejection episode in a pregnant renal transplant recipient. Pharmacotherapy, 36 (4), e18-22. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/26892892

- Case report of a 22 year old kidney transplant recipient who became pregnant 12 months after transplant and subsequently was diagnosed with biopsy confirmed 1b acute cellular rejection and antibody-mediated rejection episode. She decided to treat the rejection and continue with the pregnancy, receiving high-dose steroids, intravenous immunoglobulin and antithymocyte globulin (rabbit). She later gave birth without complication.

Ono E. et al. (2015). Immunophenotypic profile and increased risk of hospital admission for infection in infants born to female kidney transplant recipients. American Journal of Transplantation, 15 (6), 1654-65. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Immunophenotypic+Profile+and+Increased+Risk+of+Hospital+Admission+for+Infection+in+Infants+Born+to+Female+Kidney+Transplant+Recipients

- This study assessed infants born to female kidney recipients, who have been prospectively followed during their first year of life, and who were submitted to an immunological investigation at birth and a subsequent assessment at eight months. Children of kidney transplant recipients had lower CD4 positive T cells, NKT and B cell initially, but recovered to the levels of the control group by 8 months. Data from the study indicate children born of transplant recipients have a 4.4 (95%CI 1.026-15.225) times higher risk of hospital admission within the first months of life.

14.8 Uterus transplantation

York JR, et al (2023). Neonatal Outcomes after Uterus Transplantation: Dallas Uterus Transplant Study. Am J Perinatol. 40(1):42-50. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33878776/

- Prospective trial describing the hospital course and laboratory findings in the first 2 months of life of 12 infants delivered by cesarean section from mothers who had undergone uterus

transplantation. The 12 infants had neonatal courses reflecting their gestational age at delivery and did not have identified malformations or organ dysfunction.

Brännström M, et al (2023). Registry of the International Society of Uterus Transplantation: First Report. Transplantation. 107(1):10-17. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35951434/

- First report of the web-based registry developed by the International Society of Uterus Transplantation to monitor worldwide uterus transplantation activities and to serve as a repository for specific research questions. The registry contains 45 registered procedures with detailed analysis of outcomes and complications.

Wilson NK, et al (2023). Immunosuppression in Uterus Transplantation: Experience From the Dallas Uterus Transplant Study. *Transplantation*. 107(3):729-736. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/36445981/

- Review article addressing immunosuppressive therapy, rejection episodes, infections, and adverse events in 14 uterus transplant recipients. Investigators concluded that safe immunosuppression regimens can be used for uterus transplant recipients before and during pregnancy.

Porrett PM, et al. (2022). Immunologic and Infectious Concerns in Uterus Transplantation. Clin Obstet Gynecol. 65(1):37-43. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35045023/

- Review article discussing the immunosuppression regimens being used in uterus transplantation in addition to management of rejection and infectious complications in uterus transplant recipients.

Ayoubi JM, et al. (2022). Evolving clinical challenges in uterus transplantation. Reprod Biomed Online. 45(5):947-960. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35999148/

- Review article discussing donor availability, recipient suitability, surgical challenges, and recipient management after uterus transplantation and during pregnancy.

D'Amico G, et al. (2022). Immunosuppression in uterus transplantation: from transplant to delivery. Expert Opin Pharmacother. 1-17. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35723045/

- Medication selection for uterine transplant generally follows patterns established by kidney transplant. Medication dosing is dynamic as the mother undergoes physiological changes associated with pregnancy. The authors presented a flowchart that is used by their institution to help treat rejection. More research is needed to determine early markers of rejection and to create protocols to achieve tolerance.

Ralston S, et al. (2022). Uterine transplantation: A maternal-fetal medicine perspective. Semin Perinatol. 46:151522. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34844788/

- Ethical issues are important to consider in uterine transplant and are approached from a maternal-fetal medicine perspective throughout this article. Ethical principles of beneficence, non-maleficence, and autonomy are explored. The importance of informed consent is also outlined in this article.

Rosenzweig M, et al. (2021). Pregnancy after CMV infection following uterus transplantation: A case report from the Dallas Uterus Transplant Study. Transpl Infect Dis. 23(4):e13653. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34038016/

- First case report of pregnancy following uterus transplantation from CMV-positive donor into CMV-negative recipient. Patient developed an active CMV infection despite prophylactic treatment, and was treated for active infection prior to embryo transfer. Ultimately, the patient carried a healthy child to term, which suggests transplanting a CMV-positive uterus into a negative donor is possible to do safely.

Jones B, et al. (2021). Uterine Transplantation: Review of Livebirths and Reproductive Implications. Transplantation. 105:1695-1707. Retrieved From: https://pubmed.ncbi.nlm.nih.gov/33315758/

- The details of seventeen live births from uterine transplant are reviewed, in addition to clinical resources including an antenatal management algorithm. Considering the small number of participants, not to mention diverse demographics and reproductive goals, drawing definitive conclusions about reproductive outcomes is challenging. Future developments in uterine transplant should focus on publications related to reproductive outcomes.

Harris C, et al. (2021). Risk constellations, viral infections, and prophylaxis in uterine transplantation. Curr Opin Organ Transplant. 26:646-653. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34620783/

- Considering that successful pregnancy is the end goal for uterine transplant patients, the infectious risks seen with uterine transplant are important to review. The authors present options for tailoring prophylaxis options for recipients and also present a timeline of likely infections for the post-transplant course. Further data collection and reporting regarding infections in this new field will be critical for future success.

Wall A, et al. (2021). Uterus transplantation- questions and answers about the procedure that is expanding the field of solid organ transplantation. Proc(Baylor Univ Med Center). 34:581-585. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34456477/

- This article is a compilation of questions answered by the uterine transplant team at Baylor University Medical Center. The presenters addressed several challenges in the field (including surgical complications and insurance coverage) and shared their hopes for the future.

Johannesson L. et al. (2021). Decisions on second pregnancy after uterus transplantation and timing for removal of the uterus-DUETS (Dallas UtErus transplant study). BJOG, ePub ahead of print. Retrieved from: https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.16685

- Uterus transplantation is a novel and debatable topic. Uterus transplant recipients are generally limited to a recipient-graft time (RGT) of 5 years allowing for 1-2 pregnancies to occur. The Dallas Uterus Transplant Study (DUETS) reviewed important decision-making points for second pregnancies in uterus transplant recipients. These points are mainly based on the first pregnancy experience, such as recipient/couple preference, immunosuppression and renal impairment, maternal/obstetrical complications, embryo transfer and RTG, and preference for timing of hysterectomy. Aside from psychological support, these points should be considered and discussed with the patient if a second pregnancy is desired.

Putman, JM. et al. (2021) Clinical pregnancy rates and experience with in vitro fertilization after uterus transplantation: Dallas UtErus Transplant Study. Am J Obstet Gynecol, ePub ahead of print. Retrieved from: https://www.ajog.org/article/S0002-9378(21)00165-4/pdf

- Cohort observational study of 20 women examining clinical pregnancy rates among women with absolute uterine-infertility undergoing in vitro fertilization (IVF) after uterus transplant. Of the 20 women included, 14 of these patients has successful transplants and following embryo transfer, 71.4% resulted clinical pregnancy following first embryo transfer. A reduction in time from uterus transplantation to embryo transfer as well as time from uterus transplantation to clinic pregnancy was shorted compared to previous studies. The authors concluded that their approach may shorten the time from transplant to clinic pregnancy, therefore decreasing patient exposure to immunosuppression.

Benedet S. (2019). Uterus transplantation fact sheet. Acta Obstet Gynecol Scand, 98(9): 1205-1206. Retrieved from: https://obgyn.onlinelibrary.wiley.com/doi/10.1111/aogs.13674
- Review of uterus transplantation with a focus on the donor, the recipient and the child.

Kvarnstrom N. et al. (2019). Live versus deceased donor in uterus transplantation. Fertility & Sterility, 112(1), 24-27. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31277763/
- Live and deceased donor uterine transplantation pros and cons are explored in this article. Limited opportunity for deceased pre-donor uterine transplants are available. A major disadvantage to living donor uterine donation is the risk to the donor.

Jones BP. et al. (2019). Human uterine transplantation: a review of outcomes from the first 45 cases. BJOG, 126(11): 1310-1319. Retrieved from: https://obgyn.onlinelibrary.wiley.com/doi/pdfdirect/10.1111/1471-0528.15863
- Outcomes from 45 cases, including nine live births. Details include surgical, immunosuppressive and obstetric outcomes, and the feasibility of uterine transplantation.

Mahmood S. et al. (2019). DUETS (Dallas UtErus Transplant Study): The role of imaging in uterus transplantation. SAGE Open Med, 7, 2050312119875607. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31523428/
- Twenty-seven potential live uterine donors were evaluated by imaging, 9 eventually donated their uterus for transplantation. Reasons for exclusion included suboptimal quality of the vessels, presence of atherosclerosis or small size/poor quality of the uterine or utero-ovarian veins, or both, voluntary withdrawal, uterine factors, fibroids, and/or adenomyosis. Diagnostic imaging plays a crucial role in selecting appropriate potential donors, screening prospective recipients, planning the graft procedure, and following up on any graft or nongraft-related complications in both the donor and recipient after the transplantation procedure is performed.

O'Donovan L. et al. (2019). Ethical and policy issues raised by uterus transplants. Br Med Bull, 131(1), 19-28. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6821981/
- Review summarizing literature on ethical and policy issues raised by uterus transplantation.

Sampson A. et al. (2019). Uterus transplantation in women who are genetically XY. J Med Ethics, 45(10), 687-689. Retrieved from: https://jme.bmj.com/content/45/10/687
- Review of the potential medical steps necessary and associated risks for uterus transplantation in genetically XY women. Presently, the medical technology does not exist to make uterus transplantation a safe and effective option for genetically XY women; however, this group should not be excluded from participation in trials.

Tardieu A. et al. (2019). Uterus transplantation: Which indications? J Gynecol Obstet Hum Reprod, 48(1): 7-8. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30315884/
- Review article discussing the indications for uterine transplant for each uterine factor infertility etiology.

Brännström M. (2018). Current status and future direction of uterus transplantation. Current Opinion in Organ Transplantation, 23(5): 592-597. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30138148/
- Review of all cases of uterus transplantation that has been published, technical details about

surgery, and pregnancy and outcomes of live births that have been reported.

Brännström M. et al. (2018). Uterus transplantation: A rapidly expanding field. Transplantation, 102(4): 569-577. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29210893/

- Review article of absolute uterine factor infertility and update of clinical activities, achievements and challenges, and discuss areas of research interests.

Kisu I. et al. (2018). Emerging problems in uterus transplantation. BJOG: An International Journal of Obstetrics & Gynaecology 125(11): 1352-1356. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29869370/

- Review of uterus transplantation with a focus on surgical procedure, graft survival, fertility/delivery, complications, and rejection.

Testa G. et al. (2018). First live birth after uterus transplantation in the United States. Am J Transplant, 18(5), 1270-1274. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29575738/

- Report of the first birth of a healthy child following uterus transplantation in the United States, from a recipient of a uterus allograft procured from an altruistic living donor.

14.9 COVID-19, pregnancy, and transplant

Bajpai D. et al. (2020). COVID-19 pandemic and pregnancy in kidney disease. Adv Chronic Kidney Dis. 2020;27(5):397-403. Retrieved from: https://www.ackdjournal.org/article/S1548-5595(20)30121-X/abstract

- In general, pregnant women may be more vulnerable to viral pneumonia because of immunology and respiratory physiology changes in pregnancy. Pregnant patients with chronic kidney disease or kidney transplant are at a higher risk for experiencing maternal and fetal complications.

Gleeson S. et al. (2020). Lesson for the clinical nephrologist: Kidney transplant, COVID-19 and pregnancy. Journal of Nephrology: 1-3. Retrieved from: https://link.springer.com/article/10.1007/s40620-020-00897-9

- Case report of a pregnant patient who had received a kidney transplant 18 months prior to pregnancy; discussed are management of her positive COVID-19 status and, transplant medications during a high-risk pregnancy.

López M. et al. (2020). Coronavirus disease 2019 in pregnancy: a clinical management protocol and considerations for practice. Fetal Diagnosis and Therapy, 47(7), 519-528. Retrieved from: https://www.karger.com/Article/FullText/508487

- Authors include a protocol for managing COVID-19 in pregnant women.

14.10 Miscellaneous

Kallapur A, et al. (2022). Pregnancy care in solid organ transplant recipients. Int J Gynaecol Obstet. 157:502-513. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34245162/

- Most female solid organ transplant patients are within childbearing age and may regain fertility after transplant. This article is a review of current data available for management of these high risk patients before, during, and after pregnancy (including immunosuppression recommendations).

Roman A. (2021). Pregnancy after transplant- addressing mode of obstetrical delivery among solid organ transplant recipients. JAMA Netw Open. 4(10):e2127414. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34605922/

- Vaginal delivery is a reasonable delivery method for solid organ transplant recipients compared to the traditional recommendation of cesarean delivery. Labor had a high success rate (>70%) and lower composite mortality among neonates while not compromising graft survival.

Porrett PM. (2018). Biologic mechanisms and clinical consequences of pregnancy alloimmunization. American Journal of Transplantation, 18 (5), 1059-1067. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Biologic+mechanisms+and+clinical+consequences+of+pregnancy+alloimmunization

- Review article describing biological mechanisms of alloimmunization during pregnancy and the impact on donor availability later in life.

Shah S, Verma P. (2016). Overview of pregnancy in renal transplant patients. International Journal of Nephrology, 2016, 4539342. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5155089/

- Review of available literature of managing pregnancy in renal transplantation from fertility, complications during pregnancy, safety profile of immunosuppressive agents and rejection during pregnancy.

McKay DB. et al. (2008). Pregnancy after kidney transplantation. Clinical Journal of the American Society of Nephrology, 3 Suppl 2, S117-25. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/18308999

- This article reviews information to guide providers on counseling the kidney transplant recipient about risks of pregnancy for the mother and the fetus and provides information to help guide treatment of the pregnant transplant recipient.

Josephson MA. et al. (2007). Considerations in the medical management of pregnancy in transplant recipients. Advances in Chronic Kidney Disease, 14 (2), 156-67. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/17395118

- This useful article highlights counseling points for the transplant recipient in every stage of family planning. It discusses immunosuppressive medications used during pregnancy and their effects on the developing fetus. The authors also discuss pregnancy complications and their prevalence in the transplant population.

McKay DB. et al. (2005). Reproduction and transplantation: report on the AST Consensus Conference on Reproductive Issues and Transplantation. American Journal of Transplantation, 5 (7), 1592-9. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Reproduction+and+Transplantation%3A+Report+on+the+AST+Consensus+Conference+on+Reproductive+Issues+and+Trans plantation

- Summary of the consensus conference organized by the Women's Health Committee of the American Society of Transplantation held March 1-2, 2003. The article summarizes available evidence supporting consensus statements on how to determine timing of pregnancy post transplantation, comorbid factors that may influence pregnancy outcomes, preconception counseling, obstetrical management, and treatment of rejection during pregnancy. Importantly, the conference identified key gaps in knowledge to direct research in order to generate enough evidence for the creation of pregnancy in transplantation guidelines.