Emergent prelabor cesarean delivery in solid organ transplant recipients: associated risk factors and outcomes

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BACKGROUND: Pregnancies after solid organ transplant are at a higher risk of antepartum admission and pregnancy complications including cesarean delivery. Emergent prelabor cesarean delivery is associated with increased maternal and neonatal morbidity in other high-risk populations, but its incidence and impact in transplant recipients is not well-understood.

OBJECTIVE: This study aimed to characterize the risk factors and outcomes of emergency prelabor cesarean delivery in kidney and liver transplant recipients.

STUDY DESIGN: This was a retrospective cohort study of all kidney and liver transplant recipients at >20 weeks gestation enrolled in the Transplant Pregnancy Registry International between 1976 and 2019. Participants admitted antepartum who required emergency prelabor cesarean delivery were compared with those admitted antepartum who underwent nonemergent birth. The primary outcomes were severe maternal morbidity and neonatal composite morbidity. Multivariable logistic regression was conducted for neonatal composite morbidity.

RESULTS: Of 1979 births, 181 pregnancies (188 neonates) with antepartum admission were included. 51 pregnancies (53 neonates, 28%) were delivered by emergent prelabor cesarean delivery compared with 130 pregnancies (135 neonates, 72%) admitted antepartum who subsequently did not require emergent delivery. The most common indication for emergent delivery was nonreassuring fetal heart tracing (44 pregnancies /51 emergent deliveries = 86%). Pregnant people who underwent emergent prelabor cesarean delivery were less likely to deliver at a transplant center (37.3% vs 41.5%; *P*=.04) and had increased rates of chronic hypertension (33.3% vs 16.2%; *P*=.02). There was no significant difference in severe maternal morbidity (3.9% vs 4.6%; *P*=.84), though there was an increase in surgical site infection in the emergent prelabor cesarean delivery cohort (3.9% vs 0%; *P*=.02). Among those with emergent prelabor cesarean delivery, there was a significant increase in neonatal composite morbidity (43.4% vs 19.3%; *P*<.001) with earlier gestational age at delivery (33.4 vs 34.7 weeks; *P*=.02), lower birthweight (1899 g vs 2321 g; *P*<.001), lower birthweight percentile (30.3% vs 40.6%; *P*=.03), increased neonatal intensive care unit admission (52.8% vs 35.6%; *P*=.03), and increased neonatal mortality (11.3% vs 1.5%; *P*=.002). After adjusting for year of conception, race, hypertensive disorders, and fetal malformations, there was a persistent increased risk of neonatal morbidity (adjusted odds ratio, 3.01; 95% confidence interval, 1.50−6.08; *P*=.002) associated with emergent prelabor cesarean delivery after transplant.

CONCLUSION: Almost one-third of kidney and liver transplant recipients admitted antepartum had an emergency prelabor cesarean delivery, and 63% of this cohort delivered outside of a transplant center. Pregnancies after transplantation should involve multidisciplinary transplant-obstetrics collaboration to ensure optimal antepartum disease management, especially for preexisting hypertension, to prevent and mitigate obstetrical and neonatal morbidity in the setting of emergent cesarean delivery.

Keywords: Antepartum Admission, Chronic Hypertension, Emergent Cesarean, Kidney Transplant, Liver Transplant, Maternal Morbidity, Neonatal Morbidity And Mortality, Transplant Center

Introduction

Pregnancies after solid organ transplant are at a high risk of maternal and fetal complications, including hypertensive disorders of pregnancy, pulmonary embolism, antepartum admission, postpartum hemorrhage,[1−9] fetal growth restriction, prematurity, and fetal mortality.[1,2,10−16] Compounding these existing obstetrical complications is the higher rate of cesarean delivery in the transplant population. The rate of cesarean delivery in kidney transplant recipients is 56.9% to 62.6%.[1,10] For liver transplant recipients, the rate of cesarean delivery is 44% to 45.8%.[2,3,17] Emergent cesarean deliveries are at even higher risk, as emergent cesarean delivery has been identified as a risk factor associated with a greater than 4-fold increase in the risk of severe maternal morbidity during childbirth[18] and increased rates of neonatal morbidity and mortality.[19] Most emergent cesarean deliveries are performed in the setting of labor,[20] but a recent study noted that prelabor emergent cesarean deliveries were particularly prevalent in transplant recipients, occurring in 9 of 14 (64%) studied cesarean deliveries, with hypertensive disorders of pregnancy being the most common indication for delivery.[21] This study focused on anesthesia management and neither further defines or characterizes the emergent cesarean deliveries nor discusses why there was a higher rate of emergent cesarean delivery in transplant recipients. Certain other obstetrical populations have been identified to be at an increased risk of prelabor emergent cesarean delivery owing to deterioration of maternal or fetal status, including patients with advanced maternal age,[22] type I diabetes mellitus,[23] and placenta

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AJOG MFM at a Glance

Why was this study conducted?

Pregnant liver and kidney transplant recipients are at a higher risk of antepartum admission and complications. This study aimed to characterize the risk factors and outcomes of emergent prelabor cesarean deliveries in pregnant people with transplants.

Key findings

Emergent prelabor cesarean deliveries occurred in one-third of antepartum admissions in transplant recipients and was largely owing to nonreassuring fetal heart tracing. The notable risk factors for emergent prelabor cesarean delivery include chronic hypertension and delivery outside of a transplant center. There is elevated neonatal morbidity and mortality with these unplanned births.

What does this add to what is known?

Given the comorbidities in solid organ transplant recipients that contribute to increased rates of emergent prelabor cesarean delivery with associated preterm birth and neonatal morbidity, we provide additional evidence to support collaboration among maternal-fetal medicine, transplant, pediatrics, and subspecialty colleagues to care for transplant recipients and their pregnancies and establish centers of excellence.

previa.[24] Our group recently studied the indications for cesarean delivery in solid organ transplant recipients and associated outcomes over 5 decades of clinical practice.[25] However, those with emergent prelabor cesarean delivery were excluded. More data are needed in this particularly high-risk population. The objective of this study is to characterize the risk factors and outcomes of prelabor emergent cesarean delivery in kidney and liver transplant recipients. We hypothesize that transplant recipients who undergo emergent cesarean delivery during an antepartum admission will have higher rates of severe maternal morbidity (SMM) and neonatal composite morbidity.

Materials and Methods

This was a retrospective cohort registry study of data from the Transplant Pregnancy Registry International (TPRI). The TPRI and associated studies are institutional review board (Advarra Pro00008001)-approved. Pertinent demographic and outcome data were collected via telephone interview, and medical records were reviewed by trained study coordinators. All data were individually reviewed and validated for this study.

The inclusion criteria included adult kidney and liver transplant recipients with pregnancies of > 20 weeks of gestational age regardless of pregnancy outcome and antepartum hospital admission. Patients were adults >18 years at the time of delivery, though they may have received their transplant during childhood. Both kidney and liver recipients were included, given the high rates of pregnancy morbidity identified in both populations and the complexity in care management pertinent to these patients.[12] Given the small numbers of patients, it was not possible to analyze each organ separately. Other solid organ recipients (eg, heart, lung, pancreas) were reviewed in the database but were excluded from this study owing to small numbers. The 20-week gestational age threshold was chosen to exclude terminations and early pregnancy loss and capture deliveries at periviability. Antepartum admission was defined as any maternal length of stay in the hospital for all indications at any point in the pregnancy, excluding admission for labor or scheduled induction of labor. Emergent prelabor cesarean delivery was defined as an unplanned cesarean delivery conducted emergently outside of the context of labor or induction for either maternal or fetal indications. The indications for emergency delivery included fetal indications such as nonreassuring fetal heart tracing, abnormal doppler, and abnormal biophysical profile and maternal indications including uncontrolled hypertension and eclampsia. We compared pregnant patients with an antepartum admission ending in emergent prelabor cesarean delivery with patients with an antepartum admission without emergent delivery as our control group. The reason for choosing antepartum admission as the control group was based on our preliminary data review showing that most emergent prelabor cesarean deliveries occurred in patients during continuous fetal monitoring while they were inpatient; therefore, we wanted our control group to reflect a similarly high-risk population as opposed to transplant recipients being cared for in the outpatient setting.

The pertinent risk factors for emergent prelabor cesarean delivery, including demographics, comorbidities, antepartum infection, antepartum bleeding, and measures of graft function and immunosuppression, were compared. Race was self-identified. The year of conception was studied, given the anticipated differences in neonatal resuscitation capabilities over time. The transplant-to-conception interval was also quantified in years, given the previous association with graft and pregnancy outcomes.[7] Hypertensive disorders including chronic hypertension, gestational hypertension, preeclampsia, and superimposed preeclampsia were categorized based on contemporary criteria regardless of the originally assigned diagnosis at the time of registry entry. The primary outcomes of this study were SMM and neonatal composite morbidity associated with emergent prelabor cesarean delivery. SMM was defined as 1 or more of the 21 Centers for Disease Control and Prevention SMM indicators.[26] Neonatal composite morbidity was defined as 1 or more of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units adverse outcomes.[27] A secondary outcome was graft loss. Graft loss for kidney recipients was defined as the need for maintenance dialysis, repeat transplant, or death with a

functional graft. Graft loss for liver recipients was defined as the need for repeat transplant or death with a functional graft. Short-term graft loss was defined as graft loss within 3 months after delivery. For twin deliveries, each twin was treated as a separate outcome for neonatal analysis.

Statistical analysis was conducted using R Studio version 1.2 (R Core Team, 2019). Univariate categorical variables were analyzed using the chi-square and Fisher exact tests. Univariate continuous variables were analyzed using the Student *t*-test. Multivariable logistic regression was used to evaluate the independent risk factors for neonatal morbidity. The final multivariable model was adjusted for all significant univariate differences including year of conception, race, hypertensive disease, delivery at a transplant center, fetal malformations and gestational age. The generalized linear models base package in R was utilized, and both forward and backward selection using the stepAIC function created a best-fit model with the least number of variables. Goodness of fit was evaluated by the Hosmer −Lemeshow test and by graphical evaluation of model residuals. A *P* value <.05 was considered statistically significant.

Results

A total of 1979 births with known mode of delivery >20 weeks of gestation between 1976 and 2019 were screened (Figure 1). Of which, 181 pregnancies (188 neonates) with an antepartum admission were included in this study, and 51 pregnancies (53 neonates, 28%, 2 sets of twins) were delivered by emergent prelabor cesarean delivery. They were compared with the control group of 130 pregnancies (135 neonates, 72%, 5 sets of twins) born to women admitted to an antepartum service who did not require subsequent emergent delivery. Both cohorts had similar age, body mass index, and access to prenatal care (Table 1). Of note, the data available only denote whether or not the patient received prenatal care but does not further clarify early or late entry to prenatal care or the care setting. Regarding allograft factors, 75% were kidney recipients, and 25% were liver recipients (Supplemental Table 1). Both groups were treated with similar immunosuppressive regimens and had mean transplant-to- conception intervals of >2 years. Most emergent deliveries were in the setting of fetal bradycardia during inpatient monitoring, though information regarding fetal monitoring indications and interval are not available (Supplemental Table 2). Although the definitions for categorization of fetal heart tracings have changed over time, the interpretation and necessity for delivery in cases of terminal bradycardia is not expected to be altered based on year of delivery. Other indications included umbilical cord prolapse or maternal decompensation such as worsening blood pressure and eclampsia. Indications for antepartum admission and length of stay were available for 72 of 130 antepartum control participants and 20 of 51 emergent cesarean delivery participants. The most common indications for antepartum admission included preterm contractions without labor or rupture of membranes, graft dysfunction, and infection across both cohorts (Supplemental Table 3).

Regarding risk factors, patients who had prelabor emergent cesarean deliveries had increased rates of chronic hypertension (33.3% vs 16.2%; *P*=.02) and lower rates of superimposed preeclampsia (17.6% vs 36.2%; *P*=.02). Incidences of gestational hypertension and preeclampsia were not different (*P*>.05). Asian race patients had higher rates of emergent cesarean delivery (11.8% vs 1.5%; *P*=.007). Transplant recipients who underwent an emergent cesarean delivery were less likely to have delivered at a transplant center (37.3% vs 41.5%; *P*=.04) (Table 1). Most transplant centers were tertiary academic institutions.

For our primary outcome of SMM, there was no significant difference between the emergent prelabor cesarean delivery group vs the antepartum control group (3.9% vs 4.6%; *P*=.84). Regarding secondary maternal outcomes, patients who underwent an emergent prelabor cesarean delivery had increased rates of maternal surgical site infection (3.9% vs 0%; *P*=.02) (Table 2). Although the control group did include vaginal births, 76 of the 130 mothers had cesarean delivery with no surgical site infection. There were no differences in graft outcomes (Supplemental Table 1).

There was a significant increase in the primary outcome of neonatal composite morbidity in the emergent prelabor cesarean delivery cohort (43.4% vs 19.3%; *P*<.001). Emergent prelabor cesarean delivery was associated with an earlier gestational age at delivery (33.4 vs 34.7 weeks; *P*=.02), lower birthweight (1899 g vs 2321 g; *P*<.001), lower birthweight percentile (30.3% vs 40.6%; *P*=.03), and increased neonatal intensive care unit admission (52.8% vs

FIGURE 1
Flowchart of transplant recipient enrollment

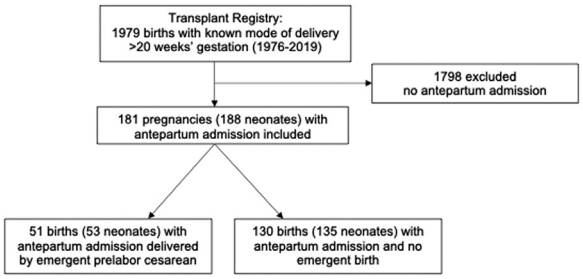

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TABLE 1
Demographics and risk factors for kidney and liver transplant recipients with antepartum admission with or without emergency prelabor cesarean delivery

Demographics and risk factors	Emergency prelabor cesarean delivery n=51 (%)	Antepartum admission n=130 (%)	*P* value
Mode of delivery			<.001
Emergent prelabor cesarean delivery	51 (100)	0 (0)	
Scheduled cesarean delivery	0 (0)	46 (35.4)	
Trial of labor to cesarean delivery	0 (0)	30 (23.1)	
Vaginal delivery	0 (0)	54 (41.5)	
Age (y), mean (SD)	29.9 (5.6)	30.3 (5.0)	.69
Body mass index (kg/m^2), mean (SD)	25.7 (5.7)	26.1 (6.4)	.80
Nulliparous	34 (66.7)	77 (59.2)	.36
Twin gestation	2 (3.9)	5 (3.8)	.98
Assisted reproductive technology	0 (0)	0 (0)	
Planned pregnancy	26 (51.0)	86 (66.2)	.06
Prenatal care	47 (92.2)	115 (88.5)	.76
Race			.03
Asian	6 (11.8)	2 (1.5)	.007
Black	4 (7.8)	8 (6.2)	.74
Other	3 (5.9)	16 (12.3)	.28
Unknown	2 (3.9)	8 (6.2)	.73
White	36 (70.6)	96 (73.8)	.71
Hypertensive disease	38 (74.5)	108 (83.1)	.02
Chronic hypertension	17 (33.3)	21 (16.2)	.02
Gestational hypertension	1 (2.0)	7 (5.4)	.45
Preeclampsia	11 (21.6)	33 (25.4)	.70
Superimposed preeclampsia	9 (17.6)	47 (36.2)	.02
Diabetes mellitus	9 (17.6)	17 (13.1)	.24
Pregestational diabetes mellitus	7 (13.7)	7 (5.4)	
Gestational diabetes mellitus	2 (3.9)	10 (7.7)	
Urinary tract infection or pyelonephritis	11 (21.6)	20 (15.4)	.32
Upper respiratory infection	4 (7.8)	7 (5.4)	.53
Aspirin use	3 (5.9)	12 (9.2)	.22
Anticoagulation	1 (2.0)	7 (5.4)	.31
Abruption	2 (3.9)	2 (1.5)	.33
Abnormal placentation	0 (0)	2 (1.5)	.67
Anemia or thrombocytopenia	3 (5.9)	11 (8.5)	.56
Antepartum bleeding	1 (2.0)	7 (5.4)	.31
Preterm prelabor rupture of membranes	2 (3.9)	4 (3.1)	.78

SD, standard deviation.

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35.6%; *P*=.03). Neonatal morbidity from respiratory distress, sepsis, and hypoxic ischemic encephalopathy was approximately double the rate in the emergent cohort than the antepartum cohort (Table 3). Emergent prelabor cesarean delivery was associated with higher neonatal mortality (11.3% vs 1.5%; *P*=.002) (Table 3).

TABLE 2
Maternal outcomes in kidney and liver transplant recipients with antepartum admission with or without emergency prelabor cesarean delivery

Pregnancy outcomes	Emergency prelabor cesarean delivery n=51 (%)	Antepartum admission n=130 (%)	*P* value
Severe maternal morbidity[a]	2 (3.9)	6 (4.6)	.84
Acute myocardial infarction	0 (0)	1 (0.8)	
Blood products transfusion	1 (2.0)	1 (0.8)	
Cardiac arrhythmia	0 (0)	1 (0.8)	
Eclampsia	1 (2.0)	0 (0)	
Hysterectomy	0 (0)	1 (0.8)	
Pulmonary edema/heart failure	0 (0)	1 (0.8)	
Sepsis	0 (0)	1 (0.8)	
Postpartum hemorrhage	1 (2.0)	2 (1.5)	.84
Intraamniotic infection	0 (0)	1 (0.8)	.53
Surgical site infection	2 (3.9)	0 (0)	.02
Postpartum readmission	1 (2.0)	2 (1.5)	.84

[a] Severe maternal mortality indicators according to the Centers for Disease Control and Prevention: acute myocardial infarction, aneurysm, acute renal failure, adult respiratory distress syndrome, amniotic fluid embolism, cardiac arrest/ventricular fibrillation, conversion of cardiac rhythm, disseminated intravascular coagulation, eclampsia, heart failure/arrest during surgery or procedure, puerperal cerebrovascular disorders, pulmonary edema/acute heart failure, severe anesthesia complications, sepsis, shock, sickle cell disease with crisis, air and thrombotic embolism, blood products transfusion, hysterectomy, temporary tracheostomy, ventilation.

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In the emergent cesarean delivery group, 6 neonates died—2 owing to multiple fetal anomalies (years 2006 and 2007), 3 owing to complications of prematurity (years 1994, 1986, and 2007), and 1 because of respiratory, kidney, and heart complications (year 1997). In the antepartum group, there were 2 neonatal deaths—1 owing to bronchopulmonary dysplasia (year 1995) and the other owing to terminal bradycardia (year 2000) with absent heart rate at delivery; for the latter, the mother developed severe preeclampsia and declined recommended delivery, resulting in deteriorating maternal status. The 6 deaths in the emergent cesarean delivery cohort had a median gestational age of 27 weeks and median birthweight of 709 g, whereas the 2 deaths in the antepartum cohort had a median gestational age of 25 weeks with a median birthweight of 680 g. Neonatal mortality remained significantly elevated even after excluding the 2 neonates with significant fetal anomalies in the emergent cohort at 7.5% (4/53) compared with 1.5% (2/135) in the nonemergent cohort (*P*=.03) (Table 3). There were not enough patients to conduct further statistical analysis of these numbers.

After adjusting for year of conception, race, hypertensive disorders, delivery at a transplant center, and fetal malformations, there was a persistent association of emergent prelabor cesarean delivery after transplant with neonatal morbidity (adjusted odds ratio [aOR], 3.01; 95% confidence interval [CI], 1.50−6.08). This persisted when further adjusting for gestational age (aOR, 2.30; 95% CI, 1.05−5.05) (Table 4).

Discussion

Principal findings

Nearly one-third of liver and kidney transplant recipients with an antepartum admission underwent a prelabor emergent cesarean delivery, most of them for nonreassuring fetal heart tracing during some form of antenatal monitoring. Emergent prelabor cesarean delivery was associated with preterm delivery at 33 weeks and was independently associated with greater than twice the rate of neonatal morbidity in this high-risk kidney and liver transplant population. There was no association between allograft type, transplant interval, or immunosuppressive regimen with emergent prelabor cesarean delivery, and the mode of delivery was not associated with peripartum rejection or short- or long-term graft loss. Preexisting chronic hypertension was a significant risk factor, as was delivery outside of a transplant center. There was a statistically significant increase in maternal surgical site infection.

Results in the context of what is known

In the context of outcomes reported for emergent prelabor cesarean delivery, a systemic review and metaanalysis found that emergent cesarean delivery was associated with significantly increased rates of neonatal morbidity and mortality and maternal complications including surgical site infection, fever, urinary infection, wound dehiscence, disseminated intravascular coagulation, and reoperation than elective cesarean delivery.[19] We found similarly worsened

TABLE 3
Neonatal outcomes in kidney and liver transplant recipients with antepartum admission with or without emergency prelabor cesarean delivery

Neonatal outcomes	Emergency prelabor cesarean delivery n=53 (%)	Antepartum admission n=135 (%)	*P* value
Gestational age (wk), mean (SD)	33.4 (3.63)	34.7 (3.27)	.02
Birthweight (g), mean (SD)	1899 (867)	2321 (732)	<.001
Birthweight percentile, mean (SD)	30.3 (25.9)	40.6 (29.1)	.03
Sex			
Female	28 (52.8)	68 (50.4)	
Male	25 (47.2)	67 (49.6)	
Fetal malformation	5 (9.4)	6 (4.4)	.19
NICU admission	28 (52.8)	48 (35.6)	.03
NICU length of stay (d), mean (SD)	21.1 (10.8)	17.1 (11.1)	.13
Neonatal composite morbidity[a]	23 (43.4)	26 (19.3)	<.001
Respiratory distress	11 (20.8)	17 (12.6)	
Intraventricular hemorrhage	1 (1.9)	2 (1.5)	
Sepsis	4 (7.5)	5 (3.7)	
Hypoxic ischemic encephalopathy	1 (1.9)	0 (0)	
Neonatal mortality	6 (11.3)	2 (1.5)	.002

NICU, neonatal intensive care unit; *SD*, standard deviation.

[a]Neonatal composite morbidity included intraventricular hemorrhage, hypoxic ischemic encephalopathy, seizure, sepsis, necrotizing enterocolitis, bronchopulmonary dysplasia, persistent pulmonary hypertension, respiratory distress syndrome, fracture, brachial plexus injury, cardiopulmonary resuscitation, or perinatal death.

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neonatal outcomes with emergent prelabor cesarean delivery after transplant, though the only significant maternal difference was surgical site infection. Transplant recipients were at a higher risk of emergent delivery independent of previously identified risk factors in nontransplant pregnancies including maternal age, diabetes mellitus, and abnormal placentation.[22–24] A unifying theme in both transplant pregnancies and other pregnancies at risk of emergent prelabor cesarean delivery is exacerbation of the underlying condition, resulting in fetal compromise with associated preterm delivery. In those with diabetes mellitus, worsening A1c is most predictive of abnormal antenatal surveillance leading to cesarean delivery with a 72% rate of prematurity at a mean gestational age of 35 weeks and 6 days.[23] In placenta previa, multiple early antepartum bleeds similarly portend the necessity for an emergency delivery at 34 weeks.[24] Our study adds to the existing literature to suggest that poor long-term vascular health owing to chronic hypertension in patients after transplant and management outside of a transplant center are 2 modifiable risk factors that are important to consider in the prevention of emergent prelabor cesarean delivery in transplant recipients.

TABLE 4
Multivariable regression of neonatal composite morbidity associated with emergent prelabor cesarean delivery in transplant recipients

Model	Unadjusted OR	*P* value	Adjusted OR	*P* value
Model 1	3.21 (1.61–6.45)	<.001	3.01 (1.50–6.08)	.002
Model 2			2.30 (1.05–5.05)	.04

Model 1: adjusted for year of conception, race, hypertensive disease, delivery at a transplant center, and fetal malformations.

Model 2: Model 1 additionally adjusted for gestational age at delivery.

OR, odds ratio.

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Clinical implications

The association of emergent prelabor cesarean delivery with chronic hypertension but not hypertensive disorders

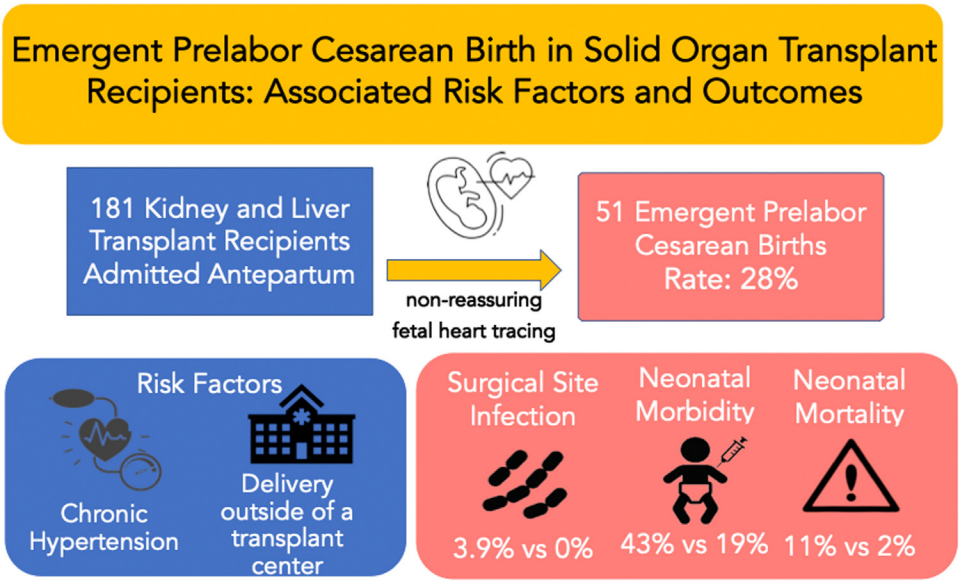
of pregnancy suggests that medically indicated preterm delivery for those with preeclampsia may mitigate the risk of an emergent cesarean delivery that otherwise would occur in those with chronic hypertension who had a later indication for delivery at 36 to 39 weeks of gestation. Interestingly, superimposed preeclampsia was not associated with increased emergent cesarean delivery. In the context of chronic hypertension, diagnosis of superimposed preeclampsia is made based on new or worsening proteinuria or presence of severe features including thrombocytopenia, renal insufficiency, transaminitis, pulmonary edema, refractory headache, or vision changes.[28] This may also relate to the indication for earlier delivery on meeting the diagnosis of superimposed preeclampsia at 37 weeks or at 34 weeks in case of severe features. The mean gestational age at delivery of 33 to 34 weeks in both cohorts suggests that pregnancies after transplantation likely experience more complications and morbidity in the late preterm or early term period. Based on these study results, obstetrical and transplant providers should thoughtfully discuss the utility of earlier delivery depending on blood pressure control and fetal status. In light of the Chronic Hypertension and Pregnancy trial that identified benefit for more aggressive blood pressure management of chronic hypertension in pregnancy and in the setting of the findings of this study, earlier and more aggressive blood pressure management targeting normotension is especially important to mitigate the risk of emergent cesarean delivery in this population.[29] Delivery at a transplant center with multidisciplinary involvement including maternal-fetal medicine, neonatology, and transplant teams may help determine the best delivery timing to optimize maternal, fetal, and allograft status.

Our findings also demonstrate the potential for improvement in the care of this high-risk population. We propose centers of excellence for care coordination for pregnant solid organ transplant recipients. A model for a center of excellence resulting in improved clinical outcomes has been shown for placenta accreta spectrum disorders.[30–32] Multidisciplinary expertise lowers the risks of massive hemorrhage, surgical complications, coagulopathy, and mortality in this high-risk group. The authors feel strongly that transplant recipients are a high-risk population at baseline with unique medical and surgical needs that require specialized expertise including graft care and immunosuppression optimization, blood pressure titration, anesthesia considerations, and infection prevention. Addressing these complications could prevent emergent cesarean delivery or mitigate associated increased maternal and neonatal morbidity, especially at the time of antepartum admission.

Research implications

Further prospective research is required to understand if antepartum care at a transplant center can reduce maternal and neonatal morbidity, as this study was conducted retrospectively and specifically looked at a particular aspect of obstetrical management. In addition, though recent studies have demonstrated no reduction in infection with postoperative antibiotics in emergent cesarean delivery,[33] it is unclear if antibiotics in the immunosuppressed transplant population would decrease this

FIGURE 2
Visual abstract



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risk of infection. More data are needed to address maternal and neonatal infection in this context.

Strengths and limitations

A major strength of our study was the availability of 43 years of data, allowing us to investigate a cohort of 51 pregnancies (53 neonates) in this study of uncommon occurrences, emergent prelabor cesarean delivery, and solid organ transplant. Women in the TPRI had close and consistent long-term follow-up. The study limitations include a small sample size in the cohorts, limiting the available analyses. Nonsignificant results and conclusions drawn from these negative findings should be interpreted with caution in this context. Registry data are subject to selection and recall bias, though the reporting bias in our study is decreased by concurrent review of medical records in addition to participant survey data. However, there were still missing data on antepartum admission indications and length of stay, excluding the ability to control for these factors, though much of this information is captured by existing data on maternal and neonatal comorbidities that exist in other parts of the registry. Although the availability of 43 years of data is a major strength of the study to capture a larger and more diverse study population, management and maternal and fetal resuscitation has vastly improved during that time. There are limitations when comparing deliveries across this time period, and it is impossible to determine if morbidity or deaths during earlier deliveries would have had different outcomes with the current standard of care. Another limitation was the lack of more specific ethnic subgroup identification. Self-identified Asian race was associated with increased emergent cesarean delivery, but "Asian" is a very heterogeneous population, so this finding can only be considered preliminary without more detailed information.[34] Better identification of ethnic subgroups could help examine the social determinants of health and structural racism that may drive risk among Asian identified pregnancies in the transplant population. Fig. 2.

Conclusions

Liver and kidney transplant recipients are at an increased risk of emergent prelabor cesarean delivery, which is associated with increased maternal surgical site infection, preterm birth, a greater than 40% rate of neonatal morbidity, and an 11% rate of neonatal mortality. We propose that pregnancies in liver and kidney transplant recipients should be cared for by multidisciplinary teams with subspecialty-transplant-obstetrics collaboration at a transplant center of excellence to mitigate the risk of emergent prelabor cesarean delivery. This may be achieved through early recognition and management of hypertensive disease, including earlier timing of delivery. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.ajogmf.2022.100799.

References

1. Deshpande NA, James NT, Kucirka LM, et al. Pregnancy outcomes in kidney transplant recipients: a systematic review and meta-analysis. Am J Transplant 2011;11:2388–404.
2. Deshpande NA, James NT, Kucirka LM, et al. Pregnancy outcomes of liver transplant recipients: a systematic review and meta-analysis. Liver Transpl 2012;18:621–9.
3. Nagy S, Bush MC, Berkowitz R, Fishbein TM, Gomez-Lobo V. Pregnancy outcome in liver transplant recipients. Obstet Gynecol 2003;102:121–8.
4. Bonanno C, Dove L. Pregnancy after liver transplantation. Semin Perinatol 2007;31:348–53.
5. Dei Malatesta MF, Rossi M, Rocca B, et al. Pregnancy after liver transplantation: report of 8 new cases and review of the literature. Transpl Immunol 2006;15:297–302.
6. Surti B, Tan J, Saab S. Pregnancy and liver transplantation. Liver Int 2008;28:1200–6.
7. Armenti VT, Constantinescu S, Moritz MJ, Davison JM. Pregnancy after transplantation. Transplant Rev (Orlando) 2008;22:223–40.
8. Pendraszewska M, Krucińska B, Pazik J, Jabiry-Zieniewicz Z, Wyzgał J. A long-term evaluation of treatment results of pregnant patients following a liver transplant. Transplant Proc 2020;52:2512–6.
9. Jain AB, Reyes J, Marcos A, et al. Pregnancy after liver transplantation with tacrolimus immunosuppression: a single center's experience update at 13 years. Transplantation 2003;76:827–32.
10. Shah S, Venkatesan RL, Gupta A, et al. Pregnancy outcomes in women with kidney transplant: metaanalysis and systematic review. BMC Nephrol 2019;20:24.
11. Coffin CS, Shaheen AAM, Burak KW, Myers RP. Pregnancy outcomes among liver transplant recipients in the United States: a nationwide case-control analysis. Liver Transpl 2010;16:56–63.
12. Kallapur A, Jang C, Yin O, Mei JY, Afshar Y. Pregnancy care in solid organ transplant recipients. Int J Gynaecol Obstet 2022;157:502–13.
13. McKay DB, Josephson MA. Pregnancy after kidney transplantation. Clin J Am Soc Nephrol 2008;3:S117–25.
14. Oliveira LG, Sass N, Sato JL, Ozaki KS, Medina Pestana JO. Pregnancy after renal transplantation-a five-yr single-center experience. Clin Transplant 2007;21:301–4.
15. Cruz Lemini MC, Ibargüengoitia Ochoa F, Villanueva González MA. Perinatal outcome following renal transplantation. Int J Gynaecol Obstet 2007;96:76–9.
16. Christopher V, Al-Chalabi T, Richardson PD, et al. Pregnancy outcome after liver transplantation: a single-center experience of 71 pregnancies in 45 recipients. Liver Transpl 2006;12:1138–43.
17. Coscia L, Constantinescu S, Moritz M, et al. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. Clin Transpl 2010;2010:65–85.
18. Guglielminotti J, Landau R, Wong CA, Li G. Patient-, hospital-, and neighborhood-level factors associated with severe maternal morbidity during childbirth: a cross-sectional study in New York state 2013-2014. Matern Child Health J 2019;23:82–91.
19. Yang XJ, Sun SS. Comparison of maternal and fetal complications in elective and emergency cesarean section: a systematic review and meta-analysis. Arch Gynecol Obstet 2017;296:503–12.
20. Lagrew DC, Bush MC, McKeown AM, Lagrew NG. Emergent (crash) cesarean delivery: indications and outcomes. Am J Obstet Gynecol 2006;194:1638–43.
21. Goto S, Fukushima R, Ozaki M. Anesthesia management in 14 cases of cesarean delivery in renal transplant patients-a single-center retrospective observational study. JA Clin Rep 2020;6:10.
22. Rosenthal AN, Paterson-Brown S. Is there an incremental rise in the risk of obstetric intervention with increasing maternal age? Br J Obstet Gynaecol 1998;105:1064–9.
23. Miailhe G, Le Ray C, Timsit J, Lepercq J. Factors associated with urgent cesarean delivery in women with type 1 diabetes mellitus. Obstet Gynecol 2013;121:983–9.
24. Pivano A, Alessandrini M, Desbriere R, et al. A score to predict the risk of emergency caesarean delivery in women with antepartum bleeding and placenta praevia. Eur J Obstet Gynecol Reprod Biol 2015;195:173–6.

25. Yin O, Kallapur A, Coscia L, et al. Mode of obstetric delivery in kidney and liver transplant recipients and associated maternal, neonatal, and graft morbidity during 5 decades of clinical practice. JAMA Netw Open 2021;4:e2127378.

26. Centers for Disease Control and Prevention. How does CDC identify severe maternal morbidity? 2021. Available at: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/smm/severe-morbidity-ICD.htm. Accessed June 29, 2021.

27. Chauhan SP, Rice MM, Grobman WA, et al. Neonatal and maternal composite adverse outcomes among low-risk nulliparous women compared with multiparous women at 39-41 weeks of gestation. Obstet Gynecol 2020;136:450–7.

28. Gestational hypertension and preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol 2020;135:e237–60.

29. Tita AT, Szychowski JM, Boggess K, et al. Treatment for mild chronic hypertension during pregnancy. N Engl J Med 2022;386:1781–92.

30. Erfani H, Fox KA, Clark SL, et al. Maternal outcomes in unexpected placenta accreta spectrum disorders: single-center experience with a multidisciplinary team. Am J Obstet Gynecol 2019;221:337.e1–5.

31. Shamshirsaz AA, Fox KA, Erfani H, et al. Multidisciplinary team learning in the management of the morbidly adherent placenta: outcome improvements over time. Am J Obstet Gynecol 2017;216:612.e1–5.

32. Silver RM, Fox KA, Barton JR, et al. Center of excellence for placenta accreta. Am J Obstet Gynecol 2015;212:561–8.

33. Dellapiana G, Levian C, Gubernick L, Burwick RM. Prophylactic postoperative antibiotics after emergent cesarean delivery and risk of postpartum infection or wound complication. J Matern Fetal Neonatal Med 2021. [Epub ahead of print].

34. Wagner SM, Bicocca MJ, Gupta M, Chauhan SP, Mendez-Figueroa H, Parchem JG. Disparities in adverse maternal outcomes among Asian women in the US delivering at term. JAMA Netw Open 2020;3:e2020180.

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