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Determinants of Perinatal Outcomes in Dialyzed and Transplanted Women in Australia

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Introduction: Drivers of adverse perinatal outcomes in pregnancies of women receiving chronic kidney replacement therapy (KRT) remain poorly understood.

Methods: Births ≥ 20 weeks of gestation in Australian women receiving KRT were analyzed for perinatal outcomes stratified by maternal KRT exposure (dialysis or transplant, analyzed separately), by linking the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) and perinatal data sets (1991–2013).

Results: Of 2,948,084 babies (1,628,181 mothers), 248 were born to mothers receiving KRT (transplant, $n = 211$; dialysis, $n = 37$), with live birth rates ≥ 94%. The perinatal death rate was 162, 62, and 9 per 1000 births in the dialysis, transplant, and non-KRT cohorts, respectively. Babies exposed to KRT had increased odds of prematurity, small-for-gestational age (SGA), poor birth condition, resuscitation, intensive care admission, and longer hospitalization, with the dialysis cohort having worse outcomes. Preterm babies of dialyzed and transplanted mothers (compared with preterm babies with no KRT exposure) experienced 1.6- to 2.7-fold higher odds for all adverse outcomes, except birthweight < 2500 g, which was 11-fold higher for the dialysis cohort. In adjusted analyses, transplanted women with better allograft function (serum creatinine ≤ 120 μmol/l) still had >10-fold higher odds of preterm birth and low birthweight and 1.8- to 4.6-fold increased odds of other adverse outcomes. In transplanted women, mediation analysis revealed that pregnancy-induced hypertension contributed only a modest proportional effect (2.5%–11.2%) on adverse outcomes.

Conclusion: Maternal dialysis and transplantation conferred excess perinatal morbidity, particularly for preterm babies, and even in women with good preconception allograft function. Pregnancy-induced hypertension is not the predominant determinant of perinatal morbidity. Preconception counseling of women with kidney disease should encompass discussion of perinatal complications.

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Pregnancy in women receiving KRT (chronic dialysis or kidney transplantation) is rare[1] but reflects an important priority for women.[2] Birth rates in Australia have remained stable for transplanted women but have risen in dialyzed women in recent years.[1] Although antenatal care has improved, these pregnancies remain at high risk of maternofetal complications.[3–6] Understanding factors driving adverse events and identifying modifiable elements will support patients and clinicians in shared decision-making during prepregnancy counseling and subsequent antenatal care.[7]

The ANZDATA has informed our basic understanding of pregnancy outcomes in women receiving dialysis or kidney transplantation,[3–5,8–10] but granular data on perinatal events and outcomes that may affect on longer-term infant health remain undefined. This study linked ANZDATA with perinatal data sets to identify a large cohort of babies born to dialyzed and transplanted women with a non-KRT comparator

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cohort, to evaluate maternal determinants of adverse perinatal outcomes in these high-risk women and help inform decision-making for women with kidney failure.

METHODS

Study Design and Population

The detailed study protocol, data set, and cohort description and births rates have been previously published.[1,11] This was a retrospective cohort study using state-level data linkage of ANZDATA Registry (1963–2016) and perinatal data sets (1991–2013) in New South Wales, Western Australia, South Australia, and the Australian Capital Territory, thereby including approximately 50% of all births in Australia from 1991 to 2013. The following 4 cohorts were identified: (i) babies of women who never received KRT at any time before December 31, 2016 (non-KRT); (ii) babies of women who started KRT after the birth event (not included in this study); (iii) babies of women who were receiving dialysis; and (iv) babies of women with a kidney transplant. The STROBE reporting guidelines were followed.[12]

Ethics Approval

Ethics approval was obtained from the Human Research Ethics Committees and the Aboriginal Human Research Ethics Committees in each jurisdiction (Supplementary Table S1).

Statistical Analysis

Comparative Analyses

Mothers receiving dialysis or transplantation were analyzed separately throughout the study given the important known clinical differences in these cohorts. Descriptive statistics were used for reporting baseline characteristics, maternal and perinatal outcomes for dialyzed or transplanted women compared with the mothers with no KRT exposure. Data were reported per mother, per parenthood event, or per birth depending on the variable. Differences were assessed using generalized Fisher exact test for categorical and Kruskal–Wallis test for continuous variables. Conception date was calculated from gestational age when it was not directly available from the data sets. SGA was defined as birthweight $<$ 10th percentile for gestational age and sex based on the Australian birth cohort.[13,14] Apgar score (appearance, pulse, grimace, activity, and respiration) $<$ 7 denoted poor birth condition and increased complications.[15] We defined preterm ($<$37 weeks of gestation), very preterm (28–32 weeks of gestation), and extremely preterm ($<$28 weeks of gestation) births.[16] Perinatal death was either stillbirth or neonatal deaths from 20 weeks of gestation to 28 days postbirth.[17] Neonatal death denoted death within 28 days of birth.[17] The most recent serum creatinine data available before conception were used. Preconception serum creatinine cutoff was at the fourth quartile with first to third quartiles delineating "better" graft function. Estimated glomerular filtration rate was calculated using Chronic Kidney Disease—Epidemiology Collaboration formulas.[18]

Univariable and multivariable logistic regression analyses were used to determine associations between dialysis and transplant exposure, preconception serum creatinine, preterm birth $<$ 37 weeks, and the risk of adverse perinatal outcomes. Generalized estimating equations grouped by mother, with an exchangeable correlation structure, were used to account for multiple pregnancies and multiple births from a single mother. This clustering was also accounted for using robust standard errors.[19] Data were expressed as odds ratios (ORs) and 95% CI.

Sources of bias, estimated causal effects, and covariates for statistical adjustment were explored using a directed acyclic graph (Figure 1). Analyses were adjusted for measured confounding factors of maternal age, pre-existing hypertension, pre-existing diabetes, socioeconomic status (based on postcode or statistical local area), parity, and multiple births (twins or higher-order births).

Perinatal outcomes for first pregnancy post-transplantation were compared with the second pregnancy post-transplantation using McNemar paired proportion test (categorical variables) and Wilcoxon signed rank test (continuous variables).

Mediation Analysis for Pregnancies in Transplanted Women

The Karlson, Holm, and Breen mediation analysis method[20,21] was used to estimate the direct effect of transplantation on adverse outcomes and the indirect effect of transplantation, mediated through pregnancy-induced hypertension, on adverse outcomes. These effects were also adjusted for factors listed previously and in Figure 1. All hypertension newly diagnosed in pregnancy after 20 weeks of gestation including pre-eclampsia were grouped as "pregnancy-induced hypertension" as per primary data sets.[22]

Unreported and Missing Data

Some data items were not collected in all jurisdictions, or in all years.[11,22] Missing data were handled by pairwise deletion for randomly missing variables. Denominators are explained in the table legends.

Analyses were conducted using Stata version 16.1 (StataCorp, College Station, TX). $P < 0.05$ was considered statistically significant. P values were not adjusted

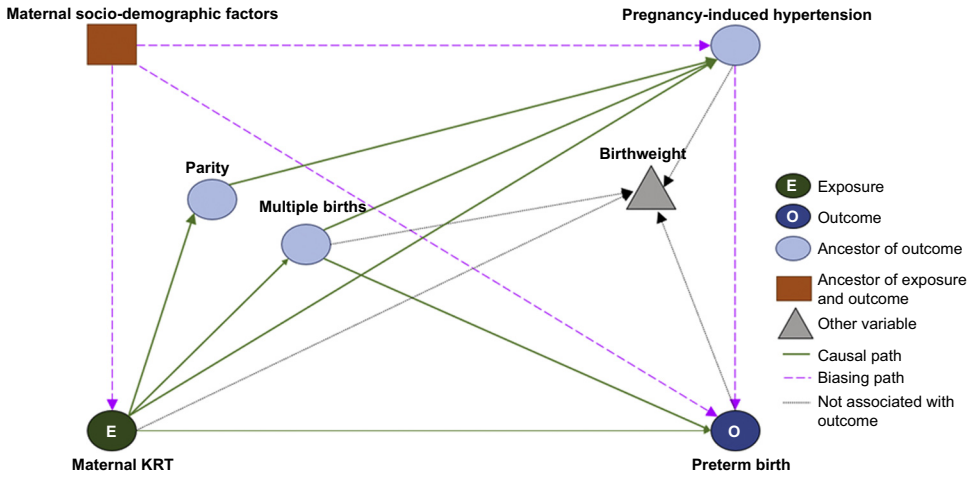


Figure 1. Directed acyclic graph for effects of maternal KRT on preterm birth. Measured maternal sociodemographic factors: age, socioeconomic status, and pre-existing diabetes/hypertension. Unmeasured factors not captured in study data sets: medications, blood pressure control, nutrition, genetic factors, environmental factors, assisted reproductive technique use, fetal assessment, antenatal kidney function, and clinician decision-making. Measured factors with excess missing data (not suitable for analysis): BMI and smoking. BMI, body mass index; KRT, kidney replacement therapy.

to account for the multiple comparisons made between groups or across outcomes.

RESULTS

Maternal Demographic Characteristics and Outcomes

From 2,948,084 births ≥ 20 weeks of gestation (1,628,181 mothers), there were 37 babies born to 31 dialyzed mothers and 211 babies born to 137 transplanted mothers. There were 9 babies born to 8 mothers with multiple organ transplants. Maternal characteristics of the dialyzed, transplanted, and non-KRT cohorts are shown in Table 1. Transplanted mothers were older with a third being 35 to 45 years of age. Dialyzed mothers were significantly less likely to be overweight or obese compared with mothers with no KRT exposure, more likely to smoke, and had significantly more occurrence of pre-existing diabetes and hypertension compared with transplanted women. Most of the mothers were Caucasian, and glomerulonephritis was the most common primary renal disease.[1] Total exposure to any KRT modality before conception was at a median of 3.2 years in dialyzed women and 8.1 years in transplanted women. Pregnancies in women receiving dialysis occurred at a median of 1.5 years after dialysis commencement, compared with 6.0 years after transplantation. Transplanted women had a median preconception serum creatinine concentration of 103 μmol/l and estimated glomerular filtration rate of 61 ml/min per 1.73 m^2.

Maternal pregnancy outcomes are shown in Table 2. Pregnancy-induced hypertension occurred 4 times more frequently in both dialyzed and transplanted groups. Gestational diabetes occurrence was similar across cohorts. The incidence of cesarean delivery was more than doubled in women receiving KRT of either modality.

Perinatal Outcomes

Perinatal Outcomes

Perinatal outcomes according to dialysis, transplant, or no KRT status are summarized in Table 3. A substantially higher percentage (~5%) of twins or higher-order births was noted in transplanted women. The vast majority of babies born to dialyzed mothers were males. Although live birth rates for pregnancies reaching ≥20 weeks of gestation were more than 94% in women with KRT exposure, this was significantly lower than women with no KRT exposure. Babies with KRT exposure had significantly lower gestational age, birthweight, length, and head circumference with 1.5- to 2-fold higher rate of SGA < 10th centile. Furthermore, although 44% of transplanted women had a term baby, more than 20% were very or extremely preterm.

Perinatal Deaths

Because perinatal data sets only include pregnancies ≥ 20 weeks of gestation, early pregnancy loss was not captured. For pregnancies reaching ≥20 weeks of gestation, the perinatal death rate was 162 per 1000 births and 62 per 1000 births in dialyzed and transplanted women, respectively, compared with 9 per 1000 births in women with no KRT exposure. Stillbirths occurred between 20 and 27 weeks of gestation in dialyzed women and 21 to 36 weeks in transplanted women. A total of 10 babies with KRT exposure died in the neonatal period, having been born at 23 to 30 weeks of gestation (Table 3).

Table 1. Maternal demographic characteristics at each parenthood event

	Non-KRT	Dialysis	Transplant	
Total number of parenthood events	***n* = 2,902,933**	***n* = 37**	***n* = 202**	
Total number of mothers	***n* = 1,627,271**	***n* = 31**	***n* = 137**	
Total number of babies	***n* = 2,946,640**	***n* = 37**	***n* = 211**	***P* value**
Maternal age at first recorded birth, yr, median (IQR)[a]	29.0 (25.0–32.9)	30.0 (25.7–33.8)	32.4 (29.0–35.4)	<0.001
Maternal age categories at birth event, *n* (%)[b,c]				<0.001
<18	39,118 (1.3)	0 (0.0)	0 (0.0)	
18–24	546,852 (18.8)	6 (16.2)	10 (5.0)	
25–34	1,773,862 (61.1)	23 (62.2)	125 (61.9)	
35–45	540,550 (18.6)	8 (21.6)	66 (32.7)	
>45	1,999 (0.1)	0 (0.0)	1 (0.5)	
BMI at conception, median (IQR)[b,d]	25.1 (22.2–29.4)	23.6 (20.9–26.2)	24.5 (21.7–28.3)	0.02
Smoked during pregnancy, *n* (%)[b,e]	396,266 (17.3)	6 (19.4)	14 (9.3)	0.04
Duration of KRT (total)-years, median (IQR)[b]	NA	3.2 (0.7–8.2)[f]	8.1 (5.1–12.6)	<0.001
Duration of KRT (latest modality)-years, median (IQR)[b]	NA	1.5 (0.7–3.5)[f]	6.0 (3.0–10.4)	<0.001
Preconception serum creatinine, μmol/l, median (IQR)[b,g]	NA	—	103 (86–121)	—
Preconception eGFR, ml/min per 1.73 m^2, median (IQR)[b,g,h]	NA	—	61.4 (50.5–76.3)	—
Low socioeconomic status[b,i,j]	717,161 (24.8)	16 (44.4)	44 (21.9)	0.09
Pre-existing diabetes, *n* (%)[b,i,k]	15,681 (0.5)	4 (10.8)	9 (4.5)	<0.001
Pre-existing hypertension, *n* (%)[b,i]	26,449 (0.9)	15 (40.5)	46 (22.8)	<0.001
Parity, *n* (%), none[b,i,l]	1,075,699 (38.9)	17 (47.2)	92 (49.2)	<0.01

BMI, body mass index; CKD-EPI, Chronic Kidney Disease—Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; IQR, interquartile range; IRSAD, Index of Relative Socioeconomic Advantage and Disadvantage; KRT, kidney replacement therapy; NA, not applicable.
[a]Data missing for *n* = 432 mothers in non-KRT.
[b]The same mother is counted multiple times if they have had multiple pregnancies.
[c]Data missing for 552 parenthood events in non-KRT.
[d]Data not available for *n* = 2,731,234 parenthood events in non-KRT; *n* = 1 in dialysis; and *n* = 91 in transplant; data not available from New South Wales and Australian Capital Territory perinatal data sets.
[e]Data missing for *n* = 605,077 parenthood events in non-KRT; *n* = 6 in dialysis; and *n* = 52 in transplant.
[f]Excluded the 15 babies born to mothers who started KRT after conception.
[g]Data missing for *n* = 1 parenthood event.
[h]eGFR calculated using the CKD-EPI equation.
[i]Maternal demographic data have been previously published.[1]
[j]Socioeconomic status: low, 1 to 3 IRSAD decile; data missing for *n* = 10,860 parenthood events in non-KRT; *n* = 1 in dialysis; and *n* = 1 in transplant.
[k]Data missing for *n* = 1 parenthood events in non-KRT.
[l]Data missing for *n* = 137,329 parenthood events in non-KRT; *n* = 1 in dialysis; and *n* = 15 in transplant.
Non-KRT: babies born to mothers who never received KRT up to the end of the study period; transplant: babies born to mothers with a kidney transplant at the time of conception; and dialysis: babies born to mothers who were receiving dialysis at the time of conception, or at birth for those commencing dialysis postconception.

Neonatal Condition at Delivery and Hospitalization

Babies of dialyzed and transplanted mothers had significantly higher rates of low (4–6) and critically low (≤3) Apgar scores at 1 and 5 minutes after birth, although birth condition improved at 5 minutes (Table 3). Subsequently, more than 60% of these babies required resuscitation therapies compared with 39% of babies with no KRT exposure. Of these babies requiring resuscitation, a significantly higher proportion required major intervention (continuous positive pressure ventilation, intermittent positive pressure ventilation, external cardiac massage and ventilation, intubation, and medications such as adrenaline). In comparison to transplanted mothers, babies of dialyzed mothers had worse birth condition across all parameters. Hospital stay was significantly longer for low birthweight and preterm babies.

Neonatal intensive care unit (NICU)/special care nursery admission was required for nearly 70% of babies of dialyzed mothers and more than half of the babies of transplanted mothers. Of babies born after 32 weeks of gestation, more NICU/special care nursery admissions were noted for babies with KRT exposure. Congenital abnormalities were reported in 1 baby born to dialyzed mothers (ventricular septum defect) and 9 babies born to transplanted mothers (intrarenal reflux bilateral, vesico-ureteric reflux, posterior urethral valves, hearing loss, and transposition of the great arteries).

Risk of Adverse Outcomes According to KRT Modality

The risks of key adverse perinatal outcomes were compared between each cohort in unadjusted and adjusted regression analyses, where event rates and sample size were adequate (Table 4). Adjusted analyses were not conducted for the dialyzed cohort owing to small numbers. Dialyzed mothers had more than 4-fold increased odds of developing pregnancy-induced hypertension and cesarean delivery, whereas transplanted mothers had more than 3-fold odds (after adjusting for confounders). The odds of very preterm birth (≤32 weeks of gestation) and birthweight < 2500 g were 30.62-fold and 46.23-fold higher for babies of dialyzed mothers and 11.40-fold and 12.28-fold higher for transplanted mothers, respectively. Similarly, we

Table 2. Maternal outcomes at each parenthood event

Maternal outcomes Total number of parenthood events	Non-KRT $n = 2{,}902{,}933$	Dialysis $n = 37$	Transplant $n = 202$	*P* value
Pregnancy-induced hypertension, *n* (%)[a]	134,407 (5.2)	8 (22.2)	48 (24.4)	<0.001
Gestational diabetes, *n* (%)[b]	124,555 (5.0)	2 (5.7)	10 (5.2)	0.85
Antepartum hemorrhage, *n* (%)[c]	77,170 (1.0)	0 (0.0)	0 (0.0)	—
Cesarean section, *n* (%)[d]	790,612 (26.8)	24 (64.9)	135 (64.0)	<0.001

KRT, kidney replacement therapy.
[a]Gestational hypertension or preeclampsia; data missing for $n = 305{,}867$ parenthood events in non-KRT, $n = 1$ in dialysis, and $n = 5$ in transplant.
[b]Data missing for $n = 401{,}077$ parenthood events in non-KRT, $n = 2$ in dialysis, and $n = 9$ in transplant.
[c]Includes placenta previa, abruptio placentae, and other causes of antepartum hemorrhage; data not available from New South Wales perinatal data sets; data not available for $n = 2{,}190{,}671$ parenthood events in non-KRT, $n = 25$ in dialysis, and $n = 125$ in transplant.
[d]Data missing for $n = 953$ parenthood events in non-KRT.

observed significantly higher odds of 5-minute Apgar score < 7, NICU admission, and needing resuscitation in babies of both dialyzed and transplanted mothers. Apart from low birthweight, which was 3.49 times higher for dialyzed women, outcomes were not statistically significantly different between the dialyzed and transplanted cohorts.

Risk of Adverse Outcomes in Transplanted Women According to Preconception Serum Creatinine

To explore pregnancy outcomes in women who may clinically be deemed as having "better" compared with "worse" preconception transplant function, we conducted an *a priori* specified analysis of women with serum creatinine concentration in the first to third quartiles compared with fourth quartile (preconception serum creatinine cutoff at 120 μmol/l), adjusted for maternal factors. Transplanted women with a preconception serum creatinine concentration of ≤120 μmol/l (better function) still had significantly worse perinatal outcomes across all parameters after adjusting for confounding factors (adjusted analyses presented in Table 5 and unadjusted analyses shown in Supplementary Table S2). In adjusted analyses, transplanted women had increased odds of preterm delivery and low birthweight (>10-fold); longer hospitalization, NICU admission, 5-minute Apgar scores < 7, and resuscitation (1.8- to 4.6-fold); and pregnancy-induced hypertension and cesarean delivery (>2-fold). When comparing maternal preconception serum creatinine more than or less than 120 μmol/l, mothers with worse function had significantly higher odds of preterm birth, low birthweight, 1-minute Apgar scores < 7, and NICU admission, but not of pregnancy-induced hypertension. The statistical difference in birthweight was not observed after adjusting for maternal factors (Table 5).

No differences were observed in transplanted women with preconception serum creatinine of <100 μmol/l versus 100 to 120 μmol/l (data not shown). In unadjusted and adjusted analyses exploring the impact of transplant-to-pregnancy interval on perinatal outcomes, no significant association was observed (Supplementary Table S3).

Mediation Analysis of the Impact of Pregnancy-Induced Hypertension on Adverse Outcomes in Transplanted Women

Given the substantially increased risks of pregnancy-induced hypertensive disorders in transplanted women, and the known impact of this on driving preterm delivery which is a key determinant of perinatal outcomes (Figure 1), we undertook mediation analysis to define the magnitude of effect of pregnancy-induced hypertension has as a mediator variable on perinatal outcomes. In unadjusted analyses, pregnancy-induced hypertension mediated 4.6% to 14.1% of the total effect on key adverse perinatal outcomes (Figure 2). After adjusting for maternal factors (maternal age, pre-existing hypertension, pre-existing diabetes, socioeconomic status, parity, and multiple births), this effect reduced to 2.5% to 11.2% (Supplementary Figure S1).

Comparison of Perinatal Outcomes for Preterm Babies According to Maternal KRT Modality

To explore the potential excess risk conferred by maternal KRT in preterm babies, perinatal outcomes were compared between preterm babies (<37 weeks of gestation) in the dialyzed, transplanted, and no KRT cohorts and are summarized in Table 6. Overall, preterm babies with KRT exposure of either modality had approximately double the odds of adverse perinatal outcomes compared with preterm babies with no KRT exposure. Babies of dialyzed mothers had 11 times increased odds of low birthweight. SGA births were noted for 23.3% ($n = 7$) of babies of dialyzed women and 18.6% ($n = 22$) of babies of transplanted women, compared with 11.3% of babies with no KRT exposure ($P = 0.006$).

Perinatal Outcomes in Multiple Pregnancies

Data for women who had >1 pregnancy while receiving dialysis or transplant are shown in Supplementary Table S4. We observed that these

Table 3. Perinatal outcomes for pregnancies ≥ 20 weeks of gestation

Outcomes Total number of babies	Non-KRT *N* = 2,946,640	Dialysis *n* = 37	Transplant *n* = 211	*P* value
Sex, *n* (%)[a,b]		0.07		
Male	1,513,465 (51.4)	28 (75.7)	108 (51.2)	
Female	1,431,974 (48.6)	9 (24.3)	103 (48.8)	
Singleton births, *n* (%)[a]	2,859,591 (98.5)	37 (100)	193 (95.5)	0.009
Birth status, *n* (%)[a,c]		<0.001		
Livebirth	2,926,962 (99.4)	35 (94.6)	204 (96.7)	
Stillbirth	18,564 (0.6)	2 (5.4)	7 (3.3)	
Neonatal death, *n* (%)[a,f]	7449 (0.3)	4 (11.4)	6 (2.9)	<0.001
Perinatal death, *n* (%)[a,c]	26,013 (0.9)	6 (16.2)	13 (6.2)	<0.001
Gestational age, wk, median (IQR)[a,d]	39 (38–40)	34 (31–35)	36 (33–38)	<0.001
Gestational age categories, *n* (%)[a,d]		<0.001		
Term (≥37 wk)	2,723,721 (92.5)	7 (18.9)	93 (44.1)	
Moderate preterm (33–36 wk)	167,423 (5.7)	17 (46.0)	73 (34.6)	
Very preterm (28–32 wk)	33,729 (1.1)	7 (18.9)	25 (11.9)	
Extremely preterm (<28 wk)	21,329 (0.7)	6 (16.2)	20 (9.5)	
Birthweight, g, median (IQR)[a,e,f]	3400 (3060–3735)	2040 (1560–2595)	2594.5 (1992.5–3070)	<0.001
Birthweight categories, *n* (%)[a,e,f]		<0.001		
Normal birthweight (2500–4499 g)	2,700,912 (92.3)	8 (22.9)	113 (55.4)	
Low birthweight (1500–2499 g)	147,463 (5.0)	19 (54.3)	64 (31.4)	
Very low birthweight (1000–1499 g)	16,185 (0.6)	2 (5.7)	12 (5.9)	
Extremely low birthweight (<1000 g)	12,107 (0.4)	5 (14.3)	15 (7.4)	
High birthweight (≥4500 g)	49,574 (1.7)	1 (2.9)	0 (0.0)	
SGA < 10th percentile, *n* (%)[a,f,g]	294,766 (10.1)	7 (20.0)	34 (16.7)	0.001
Birth length, cm, median (IQR)[a,f,h]	50 (48–52)	44 (40–48)	46 (41–49)	<0.001
Birth head circumference, cm, median (IQR)[a,f,i]	35 (34–36)	29 (28–34)	32.5 (30–34)	<0.001
Apgar score 1 min, *n* (%)[a,f,j]				<0.001
≥7 (normal)	2,596,054 (88.9)	23 (65.7)	145 (71.1)	
4–6 (low)	261,580 (8.9)	7 (20.0)	44 (21.6)	
≤3 (critical)	62,862 (2.3)	5 (14.3)	15 (7.4)	
Apgar score 5 min, *n* (%)[a,f,k]				<0.001
≥7 (normal)	2,874,780 (98.5)	31 (88.6)	185 (90.7)	
4–6 (low)	36,328 (1.2)	1 (2.9)	16 (7.8)	
≤3 (critical)	8,629 (0.3)	3 (8.6)	3 (1.5)	
Resuscitation, *n* (%)[a,f,l]				<0.001
Yes	1,000,221 (38.9)	23 (69.7)	113 (60.4)	
No	1,568,391 (61.1)	10 (30.3)	74 (39.6)	
Type of resuscitation, *n* (%)[a,f, m]				
Minor intervention				<0.01
Yes	816,902 (81.7)	10 (43.5)	71 (62.8)	
No	183,319 (18.3)	13 (56.5)	42 (37.2)	
Major intervention				<0.001
Yes	212,846 (21.3)	16 (69.6)	51 (45.1)	
No	787,375 (78.7)	7 (30.4)	62 (54.9)	

(Continued on following page)

Table 3. (Continued) Perinatal outcomes for pregnancies ≥ 20 weeks of gestation

Outcomes Total number of babies	Non-KRT *N* = 2,946,640	Dialysis *n* = 37	Transplant *n* = 211	*P* value
Hospital length of stay for baby, d, median (IQR)[a,f,n]	4 (2–5)	20 (6–29)	6 (5–18)	<0.001
NICU/SCN admission, *n* (%)[a,f,n]				<0.001
Yes	371,336 (14.7)	24 (68.6)	96 (51.3)	
No	2,154,681 (85.3)	11 (31.4)	91 (48.7)	
NICU/SCN admission by gestational age category, *n* (%)[a,f,o]				<0.001
≤32 weeks of gestation	36,212 (1.4)	10 (28.6)	36 (19.3)	
>32 weeks of gestation	335,124 (13.3)	14 (40.0)	60 (32.1)	
Congenital abnormalities, *n* (%)[a,p]				
Yes	47,217 (4.4)	1 (9.1)	9 (9.8)	0.03
No	1,025,695 (95.6)	10 (90.9)	83 (90.2)	

Apgar, appearance, pulse, grimace, activity, and respiration; IQR, interquartile range; KRT, kidney replacement therapy; NICU, neonatal intensive care unit; SCN, special care nursery; SGA, small-for-gestational age.
[a]The same mother is counted multiple times if they have had multiple pregnancies.
[b]Data missing for *n* = 869 babies in non-KRT.
[c]Data missing for *n* = 1114 babies in non-KRT.
[d]Data missing for *n* = 438 babies in non-KRT.
[e]Data missing for *n* = 721 babies in non-KRT.
[f]Includes live-born babies only.
[g]Data missing for *n* = 4580 babies in non-KRT.
[h]Data not available for *n* = 2,247,758 babies in non-KRT, *n* = 28 in dialysis, and *n* = 150 in transplant; data not available from South Australia and New South Wales perinatal data sets.
[i]Data not available for *n* = 2,247,873 babies in non-KRT, *n* = 28 in dialysis, and *n* = 150 in transplant; data not available from South Australia and New South Wales perinatal data sets.
[j]Data missing for *n* = 6466 babies in non-KRT.
[k]Data missing for *n* = 7225 babies in non-KRT.
[l]Data missing for *n* = 358,350 babies in non-KRT, *n* = 2 in dialysis, and *n* = 17 in transplant.
[m]Minor interventions included suction or oxygen; major interventions include continuous positive pressure ventilation, intermittent positive pressure ventilation, external cardiac massage and ventilation, intubation, and medications, such as adrenaline.
[n]Data not available for *n* = 1,804,687 babies in non-KRT, *n* = 22 in dialysis, and *n* = 109 in transplant; data not available from New South Wales perinatal data set.
[o]Data missing for *n* = 400,945 babies in non-KRT and *n* = 17 in transplant.
[p]Data not available for *n* = 1,873,728 babies in non-KRT, *n* = 26 in dialysis, and *n* = 119 in transplant; data not available from New South Wales and Australian Capital Territory perinatal data sets.
Total number of mothers: births to mothers never on KRT, *n* = 1,627,271; dialysis, *n* = 31; and transplant, *n* = 137.
Total number of parenthood events: births to mothers never on KRT, *n* = 2,902,933; dialysis, *n* = 37; and transplant, *n* = 202.

Table 4. Risk of adverse perinatal and pregnancy outcomes according to kidney replacement therapy modality at birth

	Transplant vs. non-KRT						Dialysis vs. non-KRT		Dialysis vs. transplant
	Unadjusted analyses			Adjusted analyses[a]			Unadjusted analyses		Unadjusted analyses,
Outcomes	*N* transplant	*N* non-KRT	OR (95% CI)	*N* transplant	*N* Non-KRT	OR (95% CI)	*N* dialysis	OR (95% CI)	OR (95% CI)
Very preterm birth (≤32 weeks of gestation)	211	2,946,202	14.96 (10.28–21.77)	195	2,796,425	11.40 (7.41–17.55)	37	30.62 (15.71–59.66)	1.91 (0.88–4.16)
Low birthweight (<2500 g)[b]	204	2,926,241	12.97 (9.48–17.74)	188	2,777,580	12.28 (8.61–17.53)	35	46.23 (21.98–97.23)	3.49 (1.68–7.25)
Length of hospital stay (≥4 d)[b]	95	1,122,275	4.62 (2.60–8.19)	81	981,847	4.30 (1.82–10.15)	-	-	-
Baby admission to NICU/SCN[b]	187	2,526,017	6.34 (4.66–8.64)	171	2,378,401	5.11 (3.64–7.17)	35	12.43 (6.17–25.02)	2.00 (0.93–4.33)
Apgar scores at 1 min (<7)[b]	204	2,920,496	3.28 (2.37–4.55)	188	2,772,096	3.11 (2.24–4.34)	35	4.15 (2.00–8.65)	1.27 (0.56–2.90)
Apgar scores at 5 min (<7)[b]	204	2,919,737	6.55 (4.08–10.53)	188	2,771,288	5.83 (3.63–9.36)	35	8.25 (2.96–22.96)	1.26 (0.40–3.90)
Resuscitation[b]	187	2,568,612	2.38 (1.73–3.28)	171	2,422,690	2.08 (1.48–2.91)	33	3.64 (1.67–7.96)	1.62 (0.65–4.07)
Cesarean section delivery	202	2,902,005	5.02 (3.59–7.02)	186	2,754,541	4.08 (2.81–5.93)	37	4.66 (2.37–9.16)	1.00 (0.472.13)
Pregnancy-induced hypertension[c]	197	2,597,066	5.78 (4.09–8.19)	181	2,450,693	3.40 (2.14–5.41)	36	5.25 (2.39–11.51)	0.92 (0.40–2.14)

Apgar, appearance, pulse, grimace, activity, and respiration; KRT, kidney replacement therapy; NICU, neonatal intensive care unit; OR, odds ratio; SCN, special care nursery.
[a]Adjusted for maternal age, pre-existing hypertension, pre-existing diabetes, socioeconomic status, parity, and multiple births.
[b]Includes live-born babies only.
[c]Includes pre-eclampsia.
-, sample size was not adequate for analysis.

subsequent pregnancies remained at high risk with 8 perinatal deaths (16.3%) in the first pregnancy and 2 stillbirths in the second pregnancy (4.3%), although the live birth rates were >95%.

Perinatal Outcomes of Special Subgroups

Preconception and Postconception Chronic Dialysis Recipients

There were 17 mothers who received chronic dialysis preconception (22 babies) and 14 mothers who commenced chronic dialysis postconception in that pregnancy (15 babies). Perinatal outcomes were similar between these groups (Figure 3). In addition, 2 neonatal deaths occurred in each group.

Peritoneal Dialysis Recipients

At delivery, 5 mothers were receiving peritoneal dialysis. Of these, 3 women started KRT for the first time in that pregnancy, 1 switched to peritoneal dialysis preconception, and 1 received peritoneal dialysis throughout. There were 4 live births, 3 were preterm with a low birthweight, all were admitted to NICU/special care nursery, 2 required resuscitation, and 1 baby died during the neonatal period.

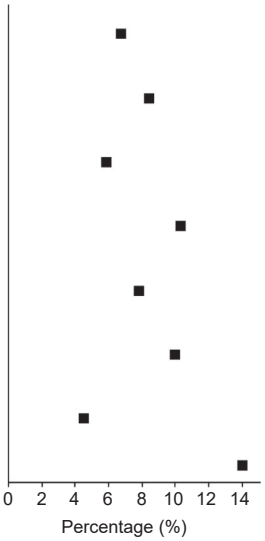
Pediatric Transplant Recipients

There were 34 babies born to 22 mothers transplanted at age ≤18 years. The median duration from transplantation to conception was 14.9 years (interquartile range: 10.4–18.6), and the median preconception serum

Table 5. Risk of adverse outcomes in transplanted women according to preconception serum creatinine

	N Serum creatinine ≤ 120 μmol/l[a]	N Serum creatinine > 120 μmol/l[a]	N Non-KRT	Serum creatinine ≤ 120 μmol/l vs. non-KRT[a]	Serum creatinine > 120 μmol/l vs. non-KRT[a]	Serum creatinine > 120 μmol/l vs. ≤120 μmol/l[a]
Outcomes				Adjusted analyses (OR [95% CI])[b]		
Preterm birth (<37 weeks of gestation)	141	53	2,796,425	12.73 (8.73–18.56)	27.41 (14.73–51.00)	2.15 (1.02–4.55)
Low birthweight (<2500 g)[c]	136	51	2,777,580	10.23 (6.64–15.75)	20.03 (10.58–37.95)	1.96 (0.91–4.23)
Length of hospital stay (≥4 d)[c]	50	31	981,847	3.20 (1.57–6.50)	9.53 (0.44–206.48)	2.98 (0.14–62.92)
Baby admission to NICU/SCN[c]	126	44	2,378,401	4.07 (2.73–6.04)	10.93 (5.38–22.23)	2.69 (1.17–6.18)
Apgar scores at 1 min (<7)[c]	136	51	2,772,096	2.29 (1.53–3.41)	6.37 (3.37–12.04)	2.79 (1.32–5.90)
Apgar scores at 5 min (<7)[b]	136	51	2,771,288	4.62 (2.54–8.42)	9.37 (4.15–21.17)	2.03 (0.71–5.76)
Resuscitation[c]	122	48	2,422,690	1.82 (1.23–2.70)	3.05 (1.49–6.26)	1.67 (0.74–3.79)
Cesarean sections	135	50	2,754,541	3.86 (2.53–5.88)	5.06 (2.62–9.80)	1.31 (0.63–2.74)
Pregnancy-induced hypertension[d]	132	48	2,450,693	2.88 (1.57–5.27)	4.96 (2.37–10.42)	1.72 (0.65–4.57)

Apgar, appearance, pulse, grimace, activity, and respiration; KRT, kidney replacement therapy; NICU, neonatal intensive care unit; OR, odds ratio; SCN, special care nursery.
[a]Cutoff of 120 μmol/l was determined based on the serum creatinine of the fourth quartile compared with the rest.
[b]Adjusted for maternal age, pre-existing hypertension, pre-existing diabetes, socioeconomic status, parity, and multiple births.
[c]Includes live-born babies only.
[d]Includes pre-eclampsia.



Outcomes	Confounding percentage[b]	N Transplant	N Non-KRT	Total effect OR (95% CI)	Direct effect OR (95% CI)	Indirect effect OR (95% CI)
Preterm birth (<37 weeks' gestation)	6.81	206	2,638,625	15.48 (11.69-20.50)	12.85 (9.70-17.01)	1.21 (1.17-1.24)
Low birthweight (<2500g)[a]	8.49	199	2,619,300	12.34 (9.27-16.44)	9.97 (7.49-13.29)	1.24 (1.20-1.28)
Caesarean sections	5.88	197	2,596,164	5.05 (3.77-6.77)	4.59 (3.43-6.16)	1.10 (1.08-1.12)
Length of hospital stay (≥4 days)[a]	10.37	90	815,349	4.47 (2.47-8.06)	3.82 (2.12-6.90)	1.17 (1.12-1.21)
Baby admission to NICU/SCN[a]	7.88	186	2,406,732	6.05 (4.52-8.09)	5.25 (3.92-7.02)	1.15 (1.13-1.18)
Apgar scores at 1 minute (<7)[a]	10.01	199	2,613,962	3.19 (2.34-4.34)	2.84 (2.09-3.86)	1.12 (1.10-1.14)
Apgar scores at 5 minutes (<7)[a]	4.57	199	2,613,141	6.37 (3.97-10.23)	5.85 (3.65-9.40)	1.09 (1.07-1.10)
Resuscitation[a]	14.08	182	2,268,741	2.35 (1.74-3.17)	2.09 (1.54-2.81)	1.13 (1.11-1.15)

Figure 2. Mediation analysis of the impact of pregnancy-induced hypertension on adverse outcomes in transplanted women (unadjusted analysis). [a]Includes live-born babies only. [b]Confounding percentage is the indirect effect as a percentage of the total effect. Apgar, appearance, pulse, grimace, activity, and respiration; KRT, kidney replacement therapy; NICU, neonatal intensive care unit; OR, odds ratio; SCN, special care nursery.

creatinine was 100 μmol/l (interquartile range: 79–126). Perinatal outcomes were generally similar to adult transplant recipients, apart from significantly higher rate of babies requiring resuscitation and NICU admission (Figure 4). There were 2 neonatal deaths (6.3%) noted.

DISCUSSION

This study harnessing the linkage of ANZDATA Registry and state-based perinatal data sets provides the most granular data to date on what drives perinatal outcomes for pregnancies in Australian women receiving dialysis or with a kidney transplant. This study confirms that these are high-risk pregnancies and delivers novel data on significantly higher rates of perinatal and neonatal death and a wide range of previously poorly reported perinatal complications, with analyses underpinned by a directed acyclic graph approach to map all *a priori* assumptions. Babies of dialyzed mothers had the highest risk, despite a live birth rate of 94%. Importantly, even in women with clinically "good" transplant function, a higher risk of perinatal complications was seen including more than 10-fold higher odds of preterm birth, and low birthweight, and 1.8- to 4.6-fold increased odds of lengthier hospitalization, NICU admission, poor birth condition, resuscitation, cesarean sections, and pregnancy-induced hypertension. This is a cohort that may be considered at lower risk, and most of the transplanted women fall into this level of kidney function—yet, they clearly have high-risk pregnancies.

A key new finding of this study was the observation that among all preterm babies, maternal dialysis or transplantation conferred approximately double the

Table 6. Risk of adverse perinatal outcomes of preterm babies (<37 weeks of gestation) according to KRT exposure

	Transplant vs. non-KRT						Dialysis vs. non-KRT		Dialysis vs. transplant
	Unadjusted analyses			Adjusted analyses[a]			Unadjusted analyses		Unadjusted analyses,
Outcomes	*N* transplant	*N* non-KRT	OR (95% CI)	*N* transplant	*N* non-KRT	OR (95% CI)	*N* dialysis	OR (95% CI)	OR (95% CI)
Low birthweight (<2500 g)[b]	111	207,635	1.82 (1.17–2.83)	107	196,698	1.95 (1.23–3.08)	28	11.08 (2.66–46.12)	5.65 (1.41–22.67)
Low Apgar (<7) at 1 min[b]	111	206,882	2.25 (1.49–3.39)	107	195,990	2.31 (1.53–3.50)	28	1.92 (0.89–4.13)	0.89 (0.40–2.01)
Low Apgar (<7) at 5 min[b]	111	206,854	2.39 (1.43–4.00)	107	195,957	2.59 (1.55–4.35)	28	2.26 (0.80–6.41)	0.92 (0.29–2.92)
Resuscitation[b]	101	185,621	1.98 (1.20–3.27)	97	174,857	1.93 (1.15–3.25)	26	2.47 (0.92–6.62)	0.88 (0.22–3.46)
Length of hospital stay (≥4 d)[b]	51	86,840	2.66 (0.83–8.60)	47	76,476	2.86 (0.85–9.58)	-	-	-
Baby admission to NICU/SCN[b]	107	193,088	1.72 (1.07–2.77)	103	182,185	1.68 (1.01–2.82)	28	2.46 (0.93–6.46)	1.33 (0.45–3.94)

Apgar, appearance, pulse, grimace, activity, and respiration; KRT, kidney replacement therapy; NICU, neonatal intensive care unit; OR, odds ratio; SCN, special care nursery.
[a]Adjusted for maternal age, pre-existing hypertension, pre-existing diabetes, socioeconomic status, parity, and multiple births.
[b]Includes live-born babies only.
-, sample size was not adequate for analysis.

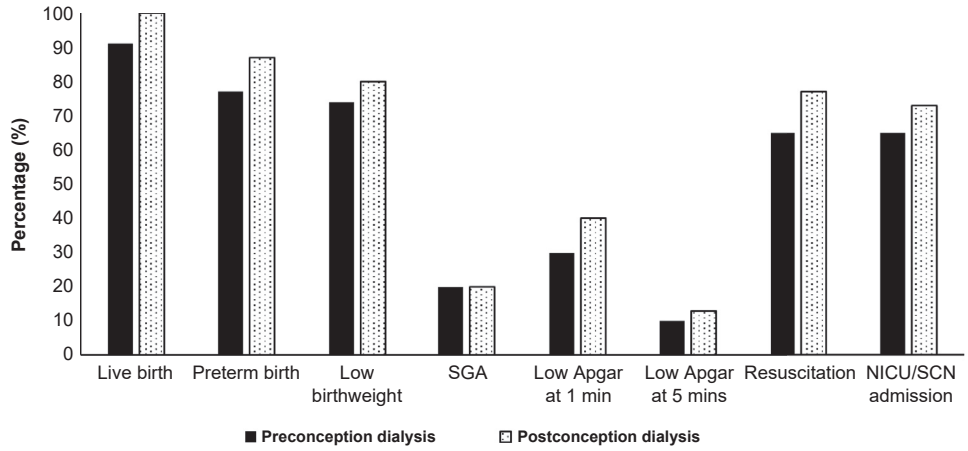


Figure 3. Perinatal outcomes of babies born to women who commenced dialysis preconception versus postconception (during that pregnancy). Preterm birth is defined as <37 weeks of gestation, and low birthweight is defined as <2500 g. Not statistically significant ($P \geq 0.05$). Preconception dialysis: $n = 22$ babies (7 mothers). Postconception dialysis: $n = 15$ babies (14 mothers). All births were ≥20 weeks of gestation. Apgar, appearance, pulse, grimace, activity, and respiration score; min, minute; NICU, neonatal intensive care unit; SCN, special care nursery; SGA, small-for-gestational age babies (<10th percentile).

odds of adverse perinatal outcomes compared with preterm babies with no KRT exposure and 11 times increased odds of low birthweight for preterm babies of dialyzed mothers.

Surprisingly, despite the increased prevalence in transplanted women, pregnancy-induced hypertension was only a modest mediator of adverse perinatal outcomes (2.5%–11.2% of total effect), indicating other, likely unmeasured, factors are involved. Collectively, these novel findings advance our ability to counsel women receiving dialysis or with a kidney transplant about pregnancy risks and impact on their babies and help clinicians understand how "safe" pregnancy is in this complex cohort.

Live birth rates for pregnancies reaching ≥20 weeks of gestation were excellent for women receiving dialysis or with a transplant; however, perinatal death was high, especially for dialyzed women. We also observed a high neonatal death rate of 11.4% in dialyzed women and 2.9% in transplanted women. This is a critically important observation that has previously been poorly captured in the ANZDATA Registry. The risks of perinatal mortality and morbidity need to be balanced with the message that most women will have a positive

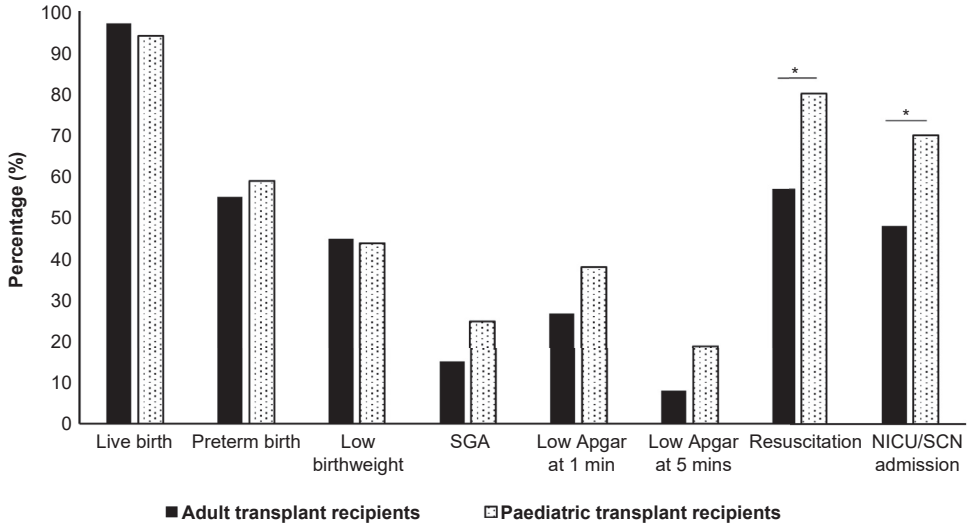


Figure 4. Perinatal outcomes of babies born to pediatric transplant recipients (≤18 years) compared with adult transplant recipients. Preterm birth is defined as <37 weeks of gestation, and low birthweight is defined as <2500 g. *$P < 0.05$. Adult transplant recipients: 177 babies (119 mothers). Pediatric transplant recipients: 34 babies (22 mothers). All births were ≥20 weeks of gestation. After adjusting for preconception serum creatinine concentration, the statistical difference remained for resuscitation ($P = 0.009$) but not for NICU/SCN ($P = 0.07$). Apgar, appearance, pulse, grimace, activity, and respiration score; min, minute; NICU, neonatal intensive care unit; SCN, special care nursery; SGA, small-for-gestational age babies (<10th percentile).

outcome. We observed similar outcomes of preterm birth and low birthweight that have been reported elsewhere.[3–6,8,10,23–26] In the Australian context, birthweight adjusted for gestational age could be calculated for the first time, and babies with maternal KRT exposure of either modality had 1.5- to 2-fold higher rate of SGA < 10th centile. The condition of neonates at birth is vital for short-term survival and long-term development of babies.[27] We found that babies of dialyzed and transplanted mothers were at higher odds of poor birth condition, needing resuscitation, NICU admission, and longer hospitalization, with babies of dialyzed women having worst outcomes. This is consistent with previous systematic reviews showing increased maternal and perinatal complications in kidney transplant recipients[25] and women receiving dialysis.[26] Maternal uremia and comorbidities are likely to contribute to poorer outcomes in dialyzed women,[28] whereas transplanted women are a highly selected cohort of women with better health and fewer comorbidities.[29]

Pregnancy-induced hypertension is an important determinant of perinatal outcomes, reflecting placental dysfunction likely driven by risk factors such as preexisting obesity, hypertension, and diabetes,[30] which are more frequent in women with kidney failure. Furthermore, chronic vascular damage from uremia and hypertension, kidney impairment, and immunosuppression exposure[31–35] will contribute to further placental dysfunction in transplanted women. Preeclampsia and pregnancy-related hypertension rates in transplanted women are high. We therefore hypothesized that pregnancy-induced hypertension would be a major mediator of adverse outcomes in transplanted women. However, the novel application of mediation analysis demonstrated only a modest effect on selected adverse outcomes, even after adjusting for contributory maternal characteristics. The lower-than-expected impact of pregnancy-induced hypertension suggests that other unmeasured factors may drive perinatal morbidity, particularly preterm delivery. These include fetal assessment, antenatal kidney function, and clinician decision-making as outlined in the directed acyclic graph in Figure 1.

We were able to conduct a direct comparison of perinatal outcomes of preterm babies with maternal KRT exposure and no KRT exposure—this is a novel approach that has not been previously possible. Although it is understood that preterm birth is substantially increased in women with kidney disease, difference in outcomes for preterm babies of mothers with kidney failure compared with other preterm babies was previously unknown. Overall, preterm babies born to transplanted women had nearly double the odds of having babies with low birthweight, lower Apgar scores, and needing resuscitation. Of particular note, preterm babies of dialyzed women had 11 times increased odds of low birthweight compared with the general preterm cohort. A higher rate of SGA births was noted for all women receiving KRT. Therefore, preterm babies with KRT exposure are likely to require additional support and care depending on the extent of prematurity and birthweight.

We hypothesized that worst perinatal outcomes are potentially driven by poorer kidney transplant function at conception given similar observation in women with chronic kidney disease.[36–38] However, we observed that women with preconception kidney function who may be considered by clinicians as "safe" (serum creatinine ≤ 120 μmol/l) still had complex pregnancies with perinatal outcomes that were significantly worse compared with women with no KRT exposure. Transplanted women regardless of their kidney transplant function should have close vigilance and monitoring throughout their pregnancy. No major statistical differences in outcomes (except preterm birth, NICU admissions, and Apgar scores) were noted for women with preconception serum creatinine > 120 μmol/l compared with women with preconception serum creatinine ≤ 120 μmol/l.

Timing in relation to KRT is a critical part of planning a pregnancy.[39] Dialyzed women who conceived after KRT start had a shorter duration of total KRT, and most became pregnant within 1.5 years of starting dialysis. The use of contraception in women receiving dialysis is low[40]; therefore, we hypothesized that these might be unplanned pregnancies where some fertility may return unexpectedly after uremia is treated. The median transplant-to-pregnancy interval was 6 years in the current study likely reflecting waiting time.[41,42] A previous meta-analysis suggested that pregnancy at 2- to 3-years post-transplantation had worse fetal outcomes[25]; however, in our study, we demonstrated that transplant-to-pregnancy interval did not affect perinatal outcomes.

We identified births in various subcohorts of women who commenced chronic dialysis pre- or post-conception, women who were transplanted during childhood or adulthood, and women who had multiple pregnancies after a successful first pregnancy, and their outcomes were similar to those of previous studies.[4,8,10] Women who had multiple pregnancies are likely a highly selected cohort because women who had favorable outcomes in 1 pregnancy are more likely to go ahead with a subsequent pregnancy.

Previous studies using the parenthood data collection within the ANZDATA Registry have laid the foundation for our understanding of pregnancy

outcomes in dialyzed[5,8] and transplanted women[3,4,9,10] in Australia; however, detailed maternal morbidity and fetal outcomes were not assessed. The major strength of this study was its ability to obtain more detailed perinatal data on this large cohort of births, enabling the development of a novel and robust data set to support the most comprehensive exploration of perinatal outcomes in women with kidney failure ever conducted in Australia. Linkage with perinatal data sets provided us access to substantially new information on maternal characteristics and perinatal outcomes enabling knowledge advancement beyond previous studies.

Despite improved data capture through linkage, the investigation was limited by potential linkage errors and missing data inherent to data linkage studies. The study period is long and ended in 2016; however, we do not believe that clinical practices have substantially changed since then. Data capture within perinatal data sets is variable from one state to another. Although the Maternity Information Matrix was utilized to pool the data sets,[22] some data items were missing, not captured or captured differently within each jurisdiction. For instance, all acute hypertensive disorders in pregnancy were coded either individually as pre-eclampsia or collectively as pregnancy-induced hypertension (or gestational hypertension) within different state-based perinatal data sets. Furthermore, we acknowledge that diagnosing pre-eclampsia is notoriously difficult in women with kidney disease, especially dialyzed women. Our birth cohort included approximately 50% of all births in Australia, but not from all jurisdictions. Despite the duration and scope of the linked data, the cohort size is small reflecting Australia's birth population and the rarity of these pregnancies. Early pregnancy losses (eg, miscarriage and surgical termination) were not captured within perinatal data sets. Kidney transplant function was calculated based on the latest available serum creatinine from ANZDATA, which may have been several years before conception in some patients. We also did not have information on proteinuria.

CONCLUSIONS

Our study using robust data sets provides new detailed data on the perinatal mortality and morbidity of babies born to dialyzed and transplanted mothers, particularly providing new data regarding birth condition and hospitalization. The perinatal outcomes for babies of dialyzed mothers were worse than for transplanted mothers across all domains. Comparison of preterm babies with and without KRT exposure revealed that KRT exposure confers risks to the baby more than those observed in preterm babies generally. Better allograft function did not mitigate the risk of perinatal morbidity, and therefore, clinicians must remain vigilant for adverse pregnancy events even in transplanted women who appear at "low risk." Pregnancy-induced hypertension was not the major mediator of adverse outcome in transplanted women indicating factors other than graft function and hypertensive disorders are involved in driving perinatal morbidity. These data are valuable in informing the complex choices women with kidney disease must make about parenthood. Risks must be conveyed factually and sensitively, but clearly articulated, so women, their partners, and families are prepared for the possibility of early delivery and perinatal complications. Early timing of pregnancy counseling and clinician support for shared decision-making are key factors in helping women navigate the path to parenthood.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

SJ, EH, CED, ES, ZL, SPM, and PC designed the study. EH and CED analyzed the data. EH, CED, SJ, ES, PC, ZL, and SPM contributed to the interpretation of the data. SJ, PC, ES, and SPM provided supervision and mentorship. EH, CED, and SJ drafted the manuscript. All authors read and approved the final version of the manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Human research ethics approvals.

Table S2. Risk of adverse outcomes transplanted women according to preconception serum creatinine (unadjusted analyses).

Table S3. Transplant-to-pregnancy interval and its association with perinatal outcomes.

Table S4. Perinatal outcomes of babies born to dialyzed and transplanted women in multiple pregnancies.

Figure S1. Mediation analysis of the impact of pregnancy-induced hypertension on adverse outcomes in transplanted women.

STROBE Checklist.

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