Pregnancy in Renal Transplant Recipients: A UK National Cohort Study

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Summary

Background and objectives Most reports of pregnancy outcome in women with kidney transplants are single-center, retrospective, and include small numbers and few are compared with controls. The aim of this study was to collect information about pregnancy outcomes among all kidney transplant recipients in the United Kingdom, managed with current antenatal and nephrologic care, and to compare these data with a contemporaneous control group.

Design, setting, participants, & measurements Pregnant women with a kidney transplant were identified through the UK Obstetric Surveillance System (UKOSS) between January 1, 2007 and December 31, 2009. Data on a comparison cohort were obtained from the UKOSS database, containing information on comparison women identified in previous studies. Outcomes were also compared with national data.

Results There were 105 pregnancies identified in 101 recipients. Median prepregnancy creatinine was 118 μmol/L. Preeclampsia developed in 24% compared with 4% of the comparison group. Median gestation at delivery was 36 weeks, with 52% of women delivering at <37 weeks, significantly higher than the national rate of 8%. Twenty-four infants (24%) were small for gestational age (<10th centile). There were two (2%) cases of acute rejection. Potential predictive factors for poor pregnancy outcome included >1 previous kidney transplant (P=0.03), first trimester serum creatinine >125 μmol/L (P=0.001), and diastolic BP >90 mmHg in the second (P=0.002) and third trimesters (P=0.05).

Conclusions Most pregnancies in the United Kingdom in women with kidney transplants are successful but rates of maternal and neonatal complications remain high.

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Introduction

Women with CKD have markedly reduced fertility with increasing severity of renal dysfunction (1). A kidney transplant rapidly restores the ability to conceive within a few months (2), and approximately 2% of women with a kidney transplant of child-bearing age become pregnant (3). Over 14,000 births to women with transplanted organs have been reported (3). Most studies reporting pregnancy outcome in women with kidney transplants are single-center–based and retrospective, may span ≥2 decades, and the majority include <50 pregnancies (4,5). Four voluntary registers have collected data (6–9) in larger numbers of women, but are reliant on self-reporting.

A recent meta-analysis assessed adverse obstetric events in women with kidney transplants, including timing of conception after transplantation (10). Although this study provides information to guide clinicians, the authors acknowledge inconsistencies in diagnostic criteria of complications, lack of adjustment for baseline differences in medical care, and underlying socioeconomic factors between countries and other unmeasured confounding issues. Furthermore, studies examining pregnancy outcome to date are likely to be restricted by reporting bias, and not all are compared with a contemporaneous control group.

The aim of this study was to collect information about pregnancy outcomes, using consistent diagnostic criteria, among renal transplant recipients in the United Kingdom, managed with current antenatal and nephrologic care over a short time period and to compare these data with a contemporaneous control group.

Materials and Methods

Data Sources and Definitions

We identified pregnant women who had previously undergone a renal transplant through the UK Obstetric Surveillance System (UKOSS) between January 1, 2007 and December 31, 2009.

The UKOSS methodology has been described in detail elsewhere (11). In brief, nominated clinicians in each consultant-led maternity unit in the United Kingdom were sent a case notification card each month and asked to report all cases. They were also asked to return cards indicating a "nil report" in order

to distinguish a nil response from a lack of response. Reporting clinicians were then asked to complete data collection forms to provide additional information about patients. All data collected were anonymous. The entire cohort of UK maternities in this study period was covered.

Data on a comparison cohort were obtained from the UKOSS database, containing information on comparison women identified in previous studies. These women were identified as the two women delivering in the same hospital immediately before a case in previous UKOSS studies (antenatal pulmonary embolism, eclampsia, and peripartum hysterectomy) (12–14), and have been shown to be representative of the general pregnancy population (15). The medical and pregnancy histories for all of the women were checked; any woman having a renal transplant history was excluded from this comparison group. For all women, data on maternal demographic characteristics and pregnancy complications, as well as maternal and infant outcomes, were collected. For the transplant cohort, we collected additional data on serum creatinine (SCr), as well as systolic and diastolic BP before the pregnancy and during each trimester. Immunosuppressive medications taken before and during pregnancy were also recorded.

National outcome data for all births in the United Kingdom were compared with the transplant cohort, using the birth statistics in 2008 (16–18) as a proxy for the period from 2007 to 2010. Where national data were unavailable, we used data from maternity hospital episode statistics for England or the British Isles Network of Congenital Anomalies Registers (BINOCAR) (19,20).

Predefined poor pregnancy outcomes were stillbirth, first or second trimester loss, termination due to a woman's medical condition, very preterm delivery (<32 weeks), congenital anomaly, or neonatal death (death up to 1 month after live birth). Small for gestational age was calculated by comparing birth weight to British 1990 growth references (21,22). Significant proteinuria was defined as >300 mg/24 h, >30 mg/mmol creatinine, or ≥2+ on standard urinalysis.

Statistical Analyses

Continuous variables were summarized as means (SDs), or medians (interquartile or entire ranges) for skewed data, and were compared by *t* test or Wilcoxon rank-sum test, respectively. Categorical variables were summarized as frequencies (percentages). Associations between categorical variables were assessed using logistic regression, chi-squared tests, or Fisher's exact tests where appropriate. Where comparable outcome data were available for women with a kidney transplant and the comparison cohort, odds ratios were adjusted for potential confounding using logistic regression. To allow for the nonindependence of multiple pregnancies from the same women, robust SEMs were calculated in the logistic regression to take into account within cluster correlation.

Highest SCr levels before birth, and in each trimester, were recorded for each woman with a kidney transplant. To estimate the changes in SCr levels during pregnancy and assess the significance of the difference in SCr levels between women with good and poor pregnancy outcomes, a generalized estimating equation approach was used to fit population-averaged panel-data models. To account for correlations in repeated measurements in SCr within each woman, we used robust (Huber–White) variance–covariance estimates at the individual level, and an autoregressive correlation structure of order 1 within women over time. SCr levels were not normally distributed, so were transformed to log-scale before entered into the model. Geometric means and 95% confidence intervals of SCr were estimated using Wald test statistics. Reduction in renal function was defined as a rise in SCr of ≥20% from the lowest level recorded during pregnancy.

Statistical analyses were carried out using STATA 11 software (StataCorp LP, College Station, TX).

Results

All 226 hospitals in the United Kingdom with consultant-led maternity units participated in the study (100%). Data collection and case ascertainment are presented in Figure 1.

A total of 105 pregnancies in 101 kidney transplant recipients were identified between January 2007 and December 2009, including four women who had two pregnancies each. Maternal characteristics are presented in Table 1. Mean age of kidney transplant recipients at pregnancy was 32 years (range, 18–44 years). Women with kidney transplants were more likely to be aged ≥35 years compared with the comparison group, and women in the comparison group were more likely to have ≥2 previous pregnancies.

Median interval from transplantation to pregnancy was 5 years (range, 2 months to 28 years; interquartile range, 2–10 years). The most common indications for transplant were reflux nephropathy (including recurrent urinary tract infections), 34 (34%), GN, 15 (15%), adult polycystic kidney disease 7 (7%) and diabetes 6 (7%). Five women (5%) also had a pancreas transplant. Over half of women (*n*=57, 56%) conceived while being treated with ≥1 antihypertensives (including three patients with angiotensin converting enzyme inhibitors).

Management

Sixteen different combinations of immunosuppressive therapies were reported (Table 2). Forty-two women (40%) took both tacrolimus and prednisolone, and 29 women (28%) took tacrolimus, azathioprine, and prednisolone before and during pregnancy. Only one woman was taking mycophenolate mofetil at conception.

Maternal Complications and Outcomes

Maternal complications and outcomes are shown in Table 3. Fourteen women (13%) had proteinuria at the start of pregnancy and 32 (30%) subsequently developed proteinuria, none of whom were diagnosed with preeclampsia. There were no significant differences in maternal characteristics between the women who developed proteinuria without preeclampsia and those who did not (data not shown).

There was no difference in risk of preeclampsia between women who had taken aspirin (*n*=7 of 32; 22%) compared with those who did not (*n*=16 of 73; 22%). However, a significantly higher proportion of those with a diastolic BP of ≥90 mmHg immediately before pregnancy were prescribed aspirin (*n*=5 of 7; 71%) compared with those

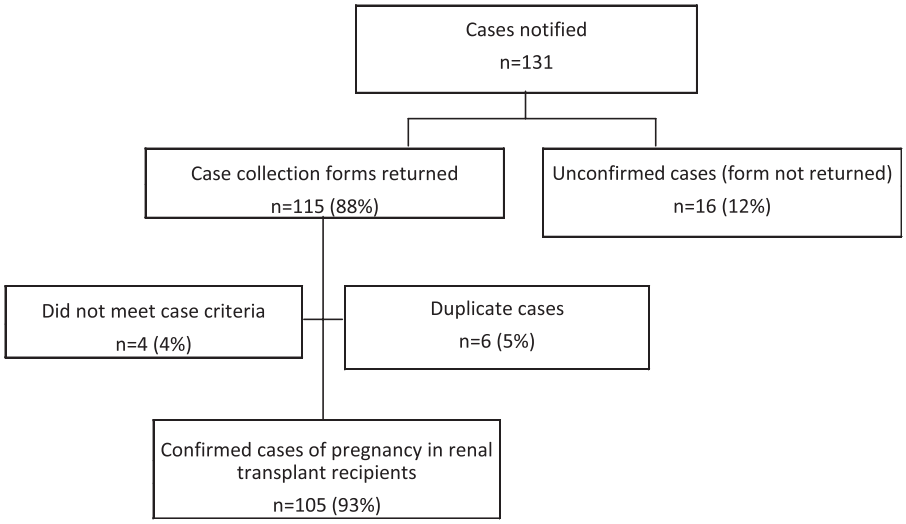

Figure 1. | **One hundred five cases were identified and unconfirmed and duplicate cases excluded.**

Table 1. Characteristics of women with a renal transplant and the comparison cohort

Demographic Characteristic	Renal Transplant Recipients (*n*=105)	Comparison Cohort (*n*=1360)	Unadjusted OR	*P* Value
Maternal age (yr)				<0.001
<20	2 (2)	69 (5)	1	
20–34	60 (57)	995 (73)	2.08 (0.50–8.71)	
≥35	43 (41)	294 (22)	5.05 (1.19–21.4)	
Ethnic group[a]				0.25
White	87 (86)	1080 (82)	1	
Nonwhite	14 (14)	244 (18)	0.68 (0.38–1.22)	
Socioeconomic status[b]				0.80
Managerial/professional	27 (30)	367 (30)	1	
Other employed	51 (58)	685 (56)	1.03 (0.64–1.68)	
Unemployed	11 (12)	169 (14)	0.85 (0.41–1.77)	
Parity				0.003
0	62 (60)	587 (43)	1	
1	37 (36)	430 (32)	0.55 (0.35–0.87)	
2+	5 (5)	339 (25)	0.47 (0.27–0.83)	
Smoking status during pregnancy				0.01
Did not smoke	89 (87)	985 (74)	1	
Smoked	13 (13)	340 (26)	0.42 (0.22–0.80)	
Body mass index				0.43
Normal (<25)	43 (47)	626 (53)	1	
Overweight (25–29.9)	31 (34)	340 (29)	1.33 (0.82–2.16)	
Obese (≥30)	18 (20)	225 (19)	1.16 (0.66–2.07)	
Multiple pregnancy				0.13
Yes	3 (3)	15 (1)	2.64 (0.75–9.27)	
No	102 (97)	1345 (99)	1	

Data are shown as *n* (%) or odds ratios (95% confidence intervals).
[a]Reported for the 101 renal transplant women, rather than 105 pregnancies, because these characteristics did not change between pregnancies.
[b]Percentages of those with data.

who had a lower BP (*n*=13 of 45; 29%) (*P*=0.04). Seventeen women (16%) who were not receiving antihypertensives at conception were subsequently prescribed them during pregnancy. Only three women developed gestational diabetes, all of whom were taking prednisolone and/or tacrolimus. Just over half of caesareans in transplant recipients (*n*=35; 57%) were of grade 1 or 2 urgency (immediate threat to life of the woman or fetus or maternal or fetal

compromise not immediately life threatening) with the remaining 43% classified as grade 3 or 4 (n=26). The most commonly reported indications for caesarean delivery before onset of labor were concern about fetal wellbeing (n=10; 23%), previous caesarean section (n=8; 19%), and deteriorating renal function (n=7; 16%). The most common indication for in-labor caesarean was fetal distress (n=12; 67%). Two women (3%) were reported to have been delivered by caesarean section solely because they had a kidney transplant, in the absence of any other clinical reason. There were no maternal deaths; however, 20% of the women (n=21) were admitted to high dependency or intensive care units compared with 1% (n=14) of the comparison group.

Allograft Function

The median SCr fell from 118 μmol/L prepregnancy to 104 μmol/L in the first and second trimesters, followed by a rise to 123 μmol/L in the third trimester. However, 49% of women (n=51) did not show a fall in SCr in the second trimester. Reduction in renal function, defined as a rise in SCr of ≥20% from the lowest level recorded during pregnancy, was reported in 38% (n=40 of 105); over three-quarters had just one episode (n=31; 79%), 15% had two to three episodes (n=6), and 5% had four or more episodes (n=2), with details for one woman missing. The cause for increased creatinine was reported in approximately half of cases (n=19; 48%); 12 were due to preeclampsia (63%) and 2 due to acute rejection (11%).

Table 2. Drugs taken before and during pregnancy

Drug	Total, n (%)
Azathioprine	61 (60)
Cyclosporine	22 (21)
Prednisolone	56 (53)
Mycophenolate mofetil	4 (4)
Tacrolimus	65 (62)
Rapamycin	2 (2)
Aspirin	32 (30)
Calcium supplements	10 (10)
Erythropoietin	3 (3)
Anticoagulants	3 (3)
Folic acid (at conception)	62 (64)

Neonatal Outcomes

Neonatal outcomes are reported in Table 4. Ten women had a first or second trimester loss or had a termination due to deteriorating renal function.

Median gestation at delivery was 36 weeks (interquartile range, 27–43 weeks). A quarter (n=13; 25%) of preterm deliveries (<37 weeks) followed induction of labor. Over three-quarters were by caesarean section (n=42; 82%), including 8 (16%) after induction of labor. The most common indications for early iatrogenic delivery were suspected renal compromise (n=18; 39%) and preeclampsia or worsening hypertension (n=11; 23%).

There were no stillbirths; however, 16 infants had at least one significant morbidity, including 10 infants with complications related to prematurity (including 2 with intraventricular hemorrhages) and a further 4 with jaundice.

Prognostic Factors for Pregnancy Outcome in Renal Transplant Recipients

About three-quarters of the transplant recipient cohort (77%) had a good pregnancy outcome, defined as any pregnancy that resulted in a live birth at >32 weeks gestation. The remaining 23% were classed as having a poor outcome (first or second trimester loss, stillbirth, neonatal death, very preterm birth <32 weeks, or a congenital anomaly). Women with ≥2 previous kidney transplants (n=20) were more likely to have poor pregnancy outcomes (P=0.03). There were no significant differences in maternal

Table 3. Pregnancy complications in women with a renal transplant and an ongoing pregnancy in the third trimester compared with the comparison cohort

Outcome	Renal Transplant Recipients (n=95)[a]	Comparison Cohort (n=1360)	Unadjusted Odds Ratio	Adjusted Odds Ratio[b]
Preeclampsia in this pregnancy[c]		n=477		
Yes	23 (24)	17 (4)	7.59 (3.87–14.9)	6.31 (2.97–13.4)
No	72 (76)	460 (96)	1	1
Gestational diabetes in this pregnancy				
Yes	3 (3)	26 (2)	1.5 (0.45–5.04)	1.21 (0.35–4.25)
No	91 (97)	1324 (98)	1	1
Induced delivery				
Yes	42 (44)	300 (22)	2.79 (1.82–4.29)	2.67 (1.73–4.13)
No	53 (56)	1057 (78)	1	1
Delivery by caesarean section				
Yes	61 (64)	326 (24)	5.69 (3.64–8.89)	4.57 (2.83–7.35)
No	34 (36)	1034 (76)	1	1

Data are shown as n (%) or odds ratios (95% confidence intervals).
[a]Ten women whose pregnancies did not continue into the third trimester are excluded from this table.
[b]Adjusted for woman's age, parity, and smoking status. Woman's age and parity are treated as continuous linear terms in the model.
[c]Including only a subset of the comparison group with data about preeclampsia.

Table 4. Pregnancy outcomes comparing to comparison cohort and national data

Outcome	Renal Transplant Cohort (n=108)[a]	Comparison Cohort (n=1375)[a]	Unadjusted Odds Ratio	Adjusted Odds Ratio[b]	National Data	Unadjusted Odds Ratio
Pregnancy outcome						
First or second trimester loss or termination	10 (9)	NA	NA	NA	NA	NA
Live birth	98 (91)	1366 (99)			NA	NA
Premature birth (<37 wk)						NA
Yes	51 (52)	114 (8)	11.7 (7.57–18.3)	12.7 (8.05–20.1)	36,558 (8)[c]	12.57 (8.48–18.6)
No	47 (48)	1235 (92)	1	1	423,475 (92)	
Very preterm birth (<32 wk)						
Yes	9 (9)	27 (2)	4.95 (2.26–10.9)	6.64 (2.88–15.3)	10,932 (2)[c]	4.15 (2.12–8.14)
No	89 (91)	1322 (98)	1	1	449,101 (98)	
Low birthweight (<2.5 kg)						
Yes	47 (48)	109 (8)	10.48 (6.73–16.3)	12.11 (7.60–19.3)	57,072 (7)	11.52 (7.77–17.1)
No	51 (52)	1239 (92)	1	1	713,201 (93)	
Very low birthweight (<1.5 kg)						
Yes	9 (9)	24 (2)	5.58 (2.52–12.4)	7.76 (3.29–18.3)	10,955 (1)	7.01 (3.58–13.7)
No	89 (91)	1324 (98)	1	1	759,318 (99)	
Small for gestational age						
Yes	24 (24)	99 (7)	4.07 (2.46–6.73)	4.87 (2.87–8.26)	10% (assumed)	2.92 (1.85–4.61)
No	74 (76)	1242 (93)	1	1		
Congenital anomaly						
Yes	4 (5)	NA	NA	NA	4308 (2)	2.46 (0.94–6.44)
No	94 (95)	NA			248,644 (100)	
Perinatal mortality						
Yes	1 (1)	10 (1)	1.38 (0.17–10.86)	1.57 (0.19–12.9)	6025 (1)	1.36 (0.00–7.74)
No	97 (99)	1335 (99)	1	1	793,022 (99)	
Neonatal unit admission						
Yes	37 (38)	NA	NA	NA	NA	NA
No	61 (62)	NA			NA	NA

Includes all fetuses/infants (N=108). Data are shown as n (%) or odds ratios (95% confidence intervals). NA, not available.

[a]Includes 3 pairs of twins in the renal transplant cohort and 15 in the comparison cohort.

[b]Adjusted for woman's age and smoking status. Woman's age was treated as a continuous linear term in the model. Parity was dropped from the model due to multicollinearity.

[c]Data from hospital episode statistics 2008–2009 (England and Wales only).

age, ethnicity, socioeconomic status, parity, smoking, body mass index, simultaneous pancreas transplant, etiology of underlying renal disease, live or cadaveric kidney donor, timing of transplantation to conception, or diastolic BP before pregnancy according to pregnancy outcomes.

Overall, women with a poor pregnancy outcome had significantly higher median creatinine, both prepregnancy and in each trimester compared with women with a good pregnancy outcome (Table 5). Taking into account the correlations in the repeated measurements in SCr within women, the overall estimated SCr levels were significantly higher in women with a poor outcome (P=0.01) (Figure 2).

However, there were no significant differences in pregnancy outcomes between women whose SCr showed the expected fall in the second trimester, compared with women whose SCr remained stable or rose in the second trimester. There was no evidence of an association between pregnancy outcome and systolic BP or use of antihypertensive treatment. Pregnancy outcome was not significantly associated with episodes of changes in renal function.

Discussion

Our data suggest that the majority of women with kidney transplants will have successful pregnancies although adverse events are common. A quarter of women have serious pregnancy complications, defined as at least one of very preterm delivery (<32 weeks' gestation) first or second trimester loss, stillbirth, neonatal death, or congenital abnormalities. Rates of preeclampsia, induction, and

Table 5. Association of pregnancy outcomes with clinical parameters during pregnancy

Characteristic	Good Pregnancy Outcome (n=81)	Poor Pregnancy Outcome (n=24)[a]	Unadjusted Odds Ratio	P Value
Preeclampsia in this pregnancy[b]				
No	61 (75)	11 (79)	1	0.79
Yes	20 (25)	3 (21)	0.44 (0.12–1.62)	
Gestational diabetes in this pregnancy[a]				
No	78 (96)	13 (100)	—	1.00
Yes	3 (4)	0 (0)	—	
Renal dysfunction during pregnancy				
No	48 (59)	15 (68)	1	0.46
Yes	33 (41)	7 (32)	0.68 (0.25–1.85)	
SCr (μmol/L), median (IQR)	113 (99–127)	148 (118–174)	—	0.01
First trimester SCr (μmol/L)[b]				
≤125	60 (82)	7 (41)	1	0.001
>125	13 (18)	10 (59)	6.59 (2.12–20.55)	
Highest proteinuria at any point in pregnancy (g/24 h)				
≤0.3	14 (27)	2 (14)	1	0.49
>0.3	38 (73)	12 (86)	2.21 (0.44–11.14)	
Lowest hemoglobin at any point in pregnancy (g/L)				
<80	8 (10)	2 (10)	1	1. 00
≥80	72 (90)	18 (90)	1 (0.20–5.12)	
Diastolic BP during pregnancy (mmHg)				
Highest diastolic BP during first trimester				
≤90	69 (92)	17 (81)	1	0.16
>90	6 (8)	4 (19)	2.71 (0.69–10.67)	
Highest diastolic BP during second trimester				
≤90	70 (88)	9 (53)	1	0.002
>90	10 (13)	8 (47)	6.22 (1.95–19.85)	
Highest diastolic BP during third trimester				
≤90	52 (64)	2 (25)	1	0.05
>90	29 (36)	6 (75)	5.38 (1.02–28.39)	

Data are shown as n (%) or odds ratios (95% confidence intervals), unless otherwise specified. SCr, serum creatinine; IQR, interquartile range.

[a]Good pregnancy outcome: Live birth at >32 weeks' gestation. Poor pregnancy outcome: First or second trimester loss, stillbirth, neonatal death, very preterm birth (<32 weeks), or a congenital anomaly.

[b]Using the subset of women who had an ongoing pregnancy in the third trimester.

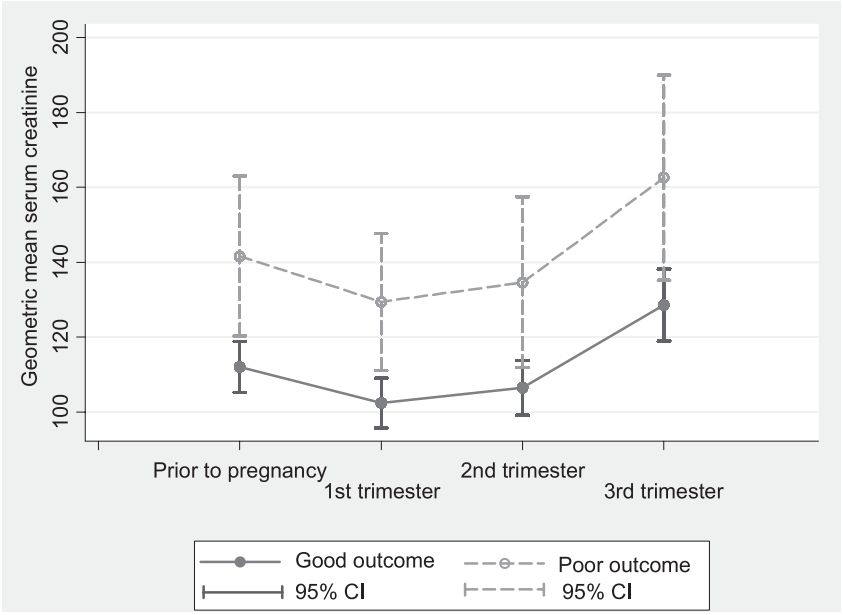

Figure 2. | Estimated mean serum creatinine and 95% confidence interval (CI) before pregnancy and in each trimester by pregnancy outcomes. Women with poor pregnancy outcome had higher serum estimated mean creatinine prior to pregnancy and in each trimester.

caesarean section were significantly higher than a comparison cohort. Rates of preterm delivery and small for gestational age infants were high compared with national data and 21% of mothers and 38% of neonates required intensive care. Previous studies have been mostly small, with data collected usually from single centers over a long time period, which may be influenced by changes in perinatal care, and protocol changes in immunosuppression regimens. Our study reflects current perinatal and nephrologic practice, and, through its national prospective design, attempts to reduce reporting bias, which is inherent in retrospective study designs. Furthermore, data analysis from 226 UK centers allowed all pregnancies in women with kidney transplants from the United Kingdom to be assessed, and therefore is unlikely to be affected by local demographic variations and individual clinicians' management of women with kidney transplants.

A recent meta-analysis of pregnancy outcome in 4706 pregnancies in 3570 women with kidney transplants (10), which predominantly included women from single centers, with deliveries before 2001 has provided important references for rates of complications, but inconsistencies in definitions for adverse events, including hypertension, preeclampsia, and preterm delivery, require these data to be interpreted with caution. Our results regarding neonatal outcome, mode of delivery, and predictive factors of pregnancy complications are comparable, adding validity to both data sets.

Our study confirms the relatively high rates of obstetric complications in women with kidney transplants, and highlights the significantly increased risk of serious adverse events. The percentage of infants born before 32 weeks' gestation was four times that expected from national data, and a quarter were small for gestational age. Previous studies with comparable outcomes included women managed more than 20 years ago (4); our data suggest little improvement in neonatal outcomes over this time.

A quarter of women developed preeclampsia compared with 4% in the comparison cohort, consistent with the findings of other reports (4). Aspirin has been shown to reduce the risk of preeclampsia in high-risk populations (23), but has never specifically been studied in women with kidney transplants. Relatively few women were prescribed aspirin, despite current UK guidelines suggesting that all women with CKD should be advised to take aspirin in pregnancy (24,25), and for all individuals post-transplantation for cardiovascular protection.

Caesarean section rates in the kidney transplants recipients were more than double the rate in the comparison group, the majority being for fetal distress with grade 1 or 2 urgency (*i.e.*, immediate threat to life of woman or fetus or maternal or fetal compromise not immediately life threatening). Many were performed preterm, and 3% were performed simply because of the presence of the graft.

Gestational diabetes mellitus (GDM) thought to be due to diabetogenic drugs, particularly tacrolimus and prednisolone, has been reported more frequently in kidney transplant recipients (6,26). The pooled incidence of GDM in women with kidney transplants in a meta-analysis of 16 studies was 8% (7% in Europe) (10). In our study, only 3% (a similar proportion to the comparison group) of women developed GDM despite over half taking tacrolimus. Others have also reported low rates of GDM in transplant recipients (4,9), which may be a consequence of different diagnostic blood glucose levels between studies, or the ethnicity of the populations included, but is otherwise unexplained.

Unfortunately, long-term assessment of graft function was not possible using UKOSS methodology, which focuses on perinatal outcomes; however, we were able to assess the proportion of women who experienced changes

in renal function during pregnancy. The expected fall in GFR with pregnancy did not occur in almost half of our cohort. Nevertheless, this was not associated with a statistically significant difference in poor pregnancy outcomes compared with women whose SCr decreased. Women with more severe renal impairment (Cr $\geq$125 μmol/L) were more likely to have poor pregnancy outcome compared with women with Cr $<$125 μmol/L, which is in keeping with other reports (4,27). A reduction in renal function in transplant recipients may be multifactorial, including preeclampsia, drug-induced, obstruction, rejection, and infection related or a physiologic return to prepregnancy values. Although 41% of women experienced at least one episode of a $>$20% rise in SCr during pregnancy, it did not appear to influence pregnancy outcomes, a finding comparable with other reports (28). Similarly, nearly a third of women developed new-onset proteinuria during pregnancy that was not associated with preeclampsia.

The UK Pregnancy Transplant Registry (UKTPR) reported that 69% of women had hypertension prepregnancy (7). We found that 56% of women conceived while taking antihypertensives, and 16% required the introduction of antihypertensives in pregnancy compared with 6% in the UKTPR report (7). Others have reported preexisting hypertension to be a predictor of pregnancy complications in kidney transplant recipients (7); however, we found no relationship between prepregnancy diastolic BP and adverse events.

We have no data regarding whether pregnancies in these women were planned; only 64% were taking folic acid at conception, suggesting either that the remainder were unplanned or that they received poor prenatal advice. Several studies have attempted to address the ideal time for conception in relation to transplantation. An interval of 12–24 months has been suggested (29); however, more recently, American Society of Transplantation Guidelines recommend that pregnancy may be considered after 1 year in women who are at low risk of complications (30) on the basis of favorable outcomes 12 months after transplant (31,32). We found no relationship between time from transplantation to conception and pregnancy outcome; however, small numbers limit the conclusions, and similar to other authors, we found no relationship between cadaveric and live organ donation and pregnancy outcome (33).

Studies reporting pregnancies in women on dialysis suggest that length of time on dialysis before pregnancy is predictive of adverse events (34), hence it might be expected that women with $>$1 kidney transplant (*i.e.*, those likely to have suffered longer periods with severe renal impairment and consequent vascular damage) would have poorer outcomes. Our study is the first to demonstrate an association between number of previous kidney transplants and poor pregnancy outcome.

Limitations

We are unable to comment on long-term graft function because this is beyond the scope of the UKOSS. The live birth rate was high (91%); however, this may reflect underreporting of early losses, for example, the 16 cases for which collection forms were not returned may represent early losses. Despite being a national study over 3 years, the number of women in the study was small, which limits the statistical power of comparisons, particularly where event rates are low and it is likely that some further real differences between the groups may have been missed.

The majority of pregnancies in the United Kingdom in women with kidney transplants are successful but rates of preeclampsia, preterm delivery, and caesarean section remain high despite improvements in obstetric, perinatal, and nephrologic care. Prescribing of aspirin in women with kidney transplants is low and nearly half of women with kidney transplants experience at least a temporary deterioration in graft function during their pregnancy. Predictive factors for poor pregnancy outcome include $\geq$2 previous kidney transplants, first trimester SCr $>$125 μmol/L, and diastolic BP $>$90 mmHg in the second and third trimesters.

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Disclosures

None.

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