Pregnancy outcomes in kidney transplant recipients: a systematic review and meta-analysis
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CRD summary
Live birth outcomes were possible among kidney transplant recipients and this trend was consistent worldwide. The high incidence of obstetric complications supported a high-risk classification of post kidney transplant pregnancies. Several limitations in the methods of synthesis and the unclear quality of the evidence mean that the conclusions of the review may not be reliable.

Authors' objectives
To estimate pooled incidences of pregnancy events, obstetric complications and delivery outcomes in kidney transplant recipients. To explore the influence of pre-pregnancy factors on pregnancy and graft outcomes, evaluate the influence of pregnancy on the allograft and assess recommendations for the ideal interval between kidney transplant and pregnancy.

Searching
MEDLINE, EMBASE and Web of Science were searched from 2000 to November 2010 for studies in English. Citations of eligible studies and relevant review articles were searched for additional studies.

Study selection
Studies that reported pregnancy outcomes, obstetric complications or delivery outcomes for kidney transplant recipients were eligible for inclusion. Studies of cancer patients and recipients of multiorgan transplant were excluded.

Mean maternal age was 29 years and the mean interval between transplantation and pregnancy was 3.2 years. Studies were conducted in a wide range of countries and regions from 1971 up to 2010.

Two reviewers independently selected the studies for inclusion. Disagreements were resolved by a third reviewer.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data on pregnancy outcomes (number of live births, pregnancies, time between kidney transplant and pregnancy, miscarriages, abortions, stillbirths and ectopic pregnancies), obstetric complications (number of women with hypertension, pre-eclampsia and gestational diabetes), delivery outcomes (number of Cesarean sections, number of preterm deliveries/before 37 weeks gestation, mean gestational age and mean birth weight) and kidney transplant outcomes (number of acute rejections during pregnancy and post-pregnancy graft survival) were extracted to calculate means, event rates and 95% confidence intervals.

Data were extracted by one reviewer and checked by a second.

Methods of synthesis
For continuous outcomes, pooled estimates and 95% confidence intervals (CIs) were calculated with a weighted Graybill-Deal estimator. For binary outcomes, pooled incidence estimates were calculated along with 95% exact binomial confidence intervals. The pooled incidence for each outcome was calculated and compared to the most recent USA general population incidence from National Vital Statistics Reports (2005 to 2006).

Pooled associations between patient characteristics categorical variables (mean maternal age, mean interval between transplant and pregnancy) and pregnancy outcomes were calculated.

Results of the review
Fifty studies (3,570 patients, 4,706 pregnancies) were included in the meta-analysis. Numbers of patients ranged from seven to 857 and numbers of pregnancies ranged from eight to 1,356.
The overall live birth rate following kidney transplant was 73.5% (95% CI 72.1 to 74.9) and was higher than the general USA population (66.7%). Live birth rates were 69% in Asia, 76% in Australia, 75% in Europe, 79% in the Middle East, 71% in North America and 76% in South America.

The overall post-kidney transplant miscarriage rate of 14.0% (95% CI 12.9 to 15.1) was lower than the USA population (17.1%). Nine point five per cent of pregnancies ended in abortion and 2.5% ended in stillbirths.

Complications of pre-eclampsia (27.0%, 95% CI 25.2 to 28.9) were higher than the general USA population (3.8%). Complications of gestational diabetes (8.0%, 95% CI 6.7 to 9.4) were higher compared to USA data (3.9%). Cesarean sections were more frequent at 56.9% (95% CI 54.9 to 58.9) compared to 31.9%. Preterm deliveries (45.6%, 95% CI 43.7 to 47.5) were more frequent compared to USA data (12.5%).

Additional outcomes data on gestational age, birth weight, rates of acute rejection and graft loss were reported. Estimates of the association between pre-pregnancy factors, mean maternal age, duration between kidney transplant and pregnancy with adverse pregnancy outcomes were reported.

**Authors’ conclusions**

Live birth outcomes were possible among kidney transplant recipients and this trend was consistent worldwide. The high incidence of obstetric complications such as hypertension, pre-eclampsia, gestational diabetes as well as delivery outcomes such as Cesarean section and preterm delivery, supported a high-risk classification of post kidney transplant pregnancies. Kidney transplant recipients also tended to deliver preterm and low birth weight babies.

**CRD commentary**

The review question and inclusion criteria were clear. Several bibliographic sources were searched. Only studies in English were included so some studies may have been missed. Measures were taken to minimise error and bias during study selection and data extraction.

No study quality assessment was reported and study designs were not reported so study quality was unclear. There may have been some overlap between the studies (acknowledged by the authors). The extent to which this may have affected the reliability of the results was unclear. It was unclear to what extent baseline characteristics were comparable between the studies as well as with the USA general population data, which may have confounded the results (acknowledged by the authors). Heterogeneity was not formally assessed but visual inspection of the forest plots suggested it may have been high (no overlap between several studies) and this suggested that pooling may not have been appropriate.

Several limitations in the methods of synthesis and the unclear quality of the evidence mean that the conclusions of the review may not be reliable.

**Implications of the review for practice and research**

**Practice**: The authors stated that a multidisciplinary team should be involved in monitoring and counselling of kidney transplant recipients before and during pregnancy.

**Research**: The authors stated that future research should investigate whether the initial period immediately following kidney transplant was a period particularly sensitive to high-risk maternal-foetal complications and evaluate potential physiological and pharmacological reasons for this sensitivity. Transplant and obstetric centres in North America should continue to share information with the National Transplantation Pregnancy Registry.

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