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Original Investigation

Kidney Disease and Maternal and Fetal Outcomes in Pregnancy

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Background: Pregnancy in kidney disease is considered high risk, but the degree of this risk is unclear. We tested the hypothesis that kidney disease in pregnancy is associated with adverse maternal and fetal outcomes.

Study Design: Retrospective study comparing pregnant women with and without kidney disease.

Setting & Participants: Using data from an integrated health care delivery system from 2000 through 2013, a total of 778 women met the criteria for kidney disease. Using a pool of 74,105 women without kidney disease, we selected 778 women to use for matches for the women with kidney disease. These women were matched 1:1 by age, race, and history of diabetes, chronic hypertension, liver disease, and connective tissue disease.

Predictor: Kidney disease was defined using the NKF-KDOQI definition for chronic kidney disease or *International Classification of Diseases, Ninth Revision* codes prior to pregnancy or serum creatinine level $>$ 1.2 mg/dL and/or proteinuria in the first trimester.

Outcomes & Measurements: Maternal outcomes included preterm delivery, delivery by cesarean section, preeclampsia/eclampsia, length of stay at hospital (>3 days), and maternal death. Fetal outcomes included low birth weight (weight $<$ 2,500 g), small for gestational age, number of admissions to neonatal intensive care unit, and infant death.

Results: Compared with women without kidney disease, those with kidney disease had 52% increased odds of preterm delivery (OR, 1.52; 95% CI, 1.16-1.99) and 33% increased odds of delivery by cesarean section (OR, 1.33; 95% CI, 1.06-1.66). Infants born to women with kidney disease had 71% increased odds of admission to the neonatal intensive care unit or infant death compared with infants born to women without kidney disease (OR, 1.71; 95% CI, 1.17-2.51). Kidney disease also was associated with 2-fold increased odds of low birth weight (OR, 2.38; 95% CI, 1.64-3.44). Kidney disease was not associated with increased risk of maternal death.

Limitations: Data for level of kidney function and cause of death not available.

Conclusions: Kidney disease in pregnancy is associated independently with adverse maternal and fetal outcomes when other comorbid conditions are controlled by matching.

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INDEX WORDS: Pregnancy; kidney disease; chronic kidney disease (CKD); decreased renal function; maternal outcomes; fetal outcomes; preterm delivery; cesarean delivery; neonatal intensive care unit (NICU) admission; low birth weight; death.

Chronic kidney disease (CKD) is a global public health problem, and the incidence and prevalence continue to increase. It is estimated that the prevalence of CKD is ~3% in women of childbearing age,[1] but kidney disease often is underappreciated in pregnancy. Pregnancy in CKD is considered high risk. It is possible that diseased kidneys are unable to adapt to the normal physiologic changes of pregnancy, resulting in adverse outcomes. Pregnancy in CKD has a high rate of adverse maternal and fetal outcomes, including miscarriage, preterm delivery, preeclampsia, and fetal death.[2] Even pregnant women with a mild decrease in glomerular filtration rate (GFR) are at an increased risk of adverse events compared with women without kidney disease.[1,2] The magnitude of this risk is unclear because most studies are small, the definitions of CKD vary, and many studies do not report important outcomes such as maternal mortality.[2] Furthermore, many of these studies did not take into account important comorbid conditions that may confound the relationship between pregnancy with kidney disease and adverse outcomes. Hence, we performed a retrospective study to provide an assessment of the risk of kidney disease during pregnancy on important maternal and fetal outcomes, including death. We tested the hypothesis that pregnant women who have kidney disease have an increased risk of adverse maternal and fetal outcomes.

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METHODS

Data Source

A retrospective study was performed using the Intermountain Healthcare Enterprise Data Warehouse, which incorporates comprehensive electronic health and administrative data.[3] Intermountain Healthcare is a nonprofit organization with 23 hospitals and more than 150 outpatient clinics and averages 130,000 admissions annually.[3] It serves the states of Utah and Idaho, and its facilities range from major adult tertiary-level care centers to small clinics and hospitals that are the only source of care in rural communities.

Cohort Definition

The study sample included all adult female patients admitted for childbirth from 2000 through 2013. All participants (women with and without kidney disease) were required to have clinical and administrative data in the Intermountain Healthcare system. Only singleton pregnancies were included; we excluded all multiple gestation pregnancies. Although several women had multiple pregnancies, only one pregnancy was used per participant in this study. In order to identify cases of preexisting kidney disease, we defined kidney disease based on data obtained prior to pregnancy or in the first trimester. Cases were identified based on *International Classification of Diseases, Ninth Revision* (*ICD-9*) code, as well as the NKF-KDOQI (National Kidney Foundation−Kidney Disease Outcomes Quality Initiative) definition of CKD (presence of kidney damage or GFR < 60 mL/min/1.73 m^2 for ≥ 3 months).[4] A woman was considered to have kidney disease if the following occurred: Charlson *ICD-9* code (582.x, 583-583.7, 585.x, 586.x, and 588.x)[5] for kidney disease existed prior to pregnancy or in the first trimester; proteinuria (based on *ICD-9* code 791)[5] existed prior to pregnancy or in the first trimester; prior to pregnancy the participant met NKF-KDOQI criteria for CKD (presence of kidney damage or GFR < 60 mL/min/1.73 m^2 for ≥ 3 months); or if serum creatinine level was >1.2 mg/dL in the first trimester. We chose serum creatinine level > 1.2 mg/dL in the first trimester as a definition of kidney disease based on previous studies using this definition.[6,7] A Charlson *ICD-9* code is a comorbidity index that is an indicator of disease burden. Categories of comorbid conditions are included based on individual *ICD-9* codes and the patient must be actively managed for the condition in order for it to be included as a comorbid condition.[5]

Seven hundred seventy-eight women met the criteria for kidney disease (Table S1, available as online supplementary material). Using a pool of 74,105 women without kidney disease, we selected 778 women to use for matches for the women with kidney disease. Women with kidney disease were matched in a 1:1 fashion by age, race, and history of diabetes, chronic hypertension, liver disease, and connective tissue disease to women without kidney disease. An exact or approximate (within 2 years) match criterion was used for age. A woman was considered to have diabetes, liver disease, and/or a connective tissue disorder if a Charlson *ICD-9* code for these comorbid conditions existed. Connective tissue disorders included lupus, Sjögren syndrome, dermatomyositis, polymyositis, rheumatoid arthritis, unspecified connective tissue diseases, polymyalgia rheumatic, and other inflammatory polyarthropathies. Hypertension prior to pregnancy also was defined by *ICD-9* code.

Outcomes

Our main objective was to examine whether women with kidney disease have a higher risk of adverse maternal and fetal outcomes compared with women without kidney disease. Outcomes were chosen based on previous studies examining adverse outcomes in pregnancy.[2] Adverse maternal outcomes were defined as: (1) gestational age at birth (4 different dichotomous groupings: (a) preterm delivery (delivery $<$ 37 weeks' gestation), (b) extremely preterm ($<$28 weeks' gestation), (c) early preterm (28-33 weeks' gestation), and (d) late preterm (34-36 weeks' gestation); (2) delivery by cesarean section; (3) longer length of stay at the hospital (length of stay $>$ 3 days); (4) combined outcome of preeclampsia and eclampsia (outcome was combined given the low number of patients with eclampsia); and (5) maternal death (because there was only one death within 1 year of delivery, we defined maternal death as death occurring at any time). Adverse fetal outcomes were defined as: (1) low birth weight ($<$2,500 g), (2) small-for-gestational-age infant (infant $<$ 10th percentile of birth weight for given gestational age), and (3) combined outcome of number of admissions to the neonatal intensive care unit (NICU) and fetal death (death during the hospitalization).

Statistical Analysis

Descriptive statistics were used to summarize characteristics of women with and without kidney disease. Percentages were used for categorical data and mean ± standard deviation were used for continuous data. Two-sample *t* tests were used to compare characteristics and outcomes between the 2 groups. Conditional logistic regression was used to examine the association between kidney disease and maternal and fetal outcomes. We considered a finding to be statistically significant for 2-sided $P < 0.05$. All statistical analyses were performed with SAS software, version 9.13 (SAS Institute Inc).

RESULTS

Study Participants

Seven hundred seventy-eight women met the criteria for kidney disease (Table S1). These women were matched 1:1 by race and history of diabetes, chronic hypertension, liver disease, and connective tissue disease and near-matched (within 2 years) by age with 778 women without kidney disease. As seen in Table 1, the women with kidney disease were well matched with women without kidney disease. Mean age was 28.66 ± 5.40 years for women with kidney disease versus 28.67 ± 5.39 years for women without kidney disease. In the entire study population, there were 209 (13.4%) preterm deliveries, 458 (29.4%) cesarean sections, 138 (8.9%) cases of preeclampsia/eclampsia, 17 (1.1%) maternal deaths, 149 (9.6%) infants with low birth weight, 118 (7.6%) admissions to the NICU, and 3 (0.2%) infant deaths.

Maternal Outcomes

Maternal and fetal outcomes in women with and without kidney disease are shown in Table 2. Mean gestational ages at delivery in women with and without kidney disease were 37.5 ± 2.5 and 38.2 ± 1.8 weeks, respectively ($P < 0.001$). Women with kidney disease were more likely to have preterm deliveries and delivery by cesarean sections compared with women without kidney disease. There was no difference in hospital length of stay and incidence of maternal death between the 2 groups. Mean times to maternal death after delivery in women with and without kidney disease were 5.2 ± 3.8 and 5.2 ± 4.4