OBSTETRICS

End-stage renal disease after hypertensive disorders in pregnancy

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OBJECTIVE: The purpose of this study was to determine the long-term postpartum risk of end-stage renal disease in women with hypertensive disorders in pregnancy. Although most women with hypertensive disorders in pregnancy recover after delivery, some may experience acute renal failure.

STUDY DESIGN: We searched Taiwan's National Health Insurance Research Database to identify women with hypertensive disorders in pregnancies and deliveries between 1998 and 2002. All cases were followed for a maximum of 11 years (median, 9 years; interquartile range, 7.79—10.02 years) to estimate the incidence of end-stage renal disease; Cox regression analysis that was adjusted for potential confounding was used to determine the relative risk.

RESULTS: Of the 13,633 women with hypertensive disorders in pregnancy, 46 experienced end-stage renal disease. Women with hypertensive disorders in pregnancy had a risk of end-stage renal disease that was 10.64 times greater than did women without them (95% confidence interval [CI], 7.53—15.05). The risk was highest in women with a history of preeclampsia superimposed on chronic hypertension (hazard ratio, 44.72; 95% CI, 22.59—88.51). Women with gestational hypertension had a higher risk of end-stage renal disease than did women without hypertensive disorders in pregnancy (hazard ratio, 5.82; 95% CI, 2.15—15.77).

CONCLUSION: Women with hypertensive disorders in pregnancy have a higher risk of postpartum end-stage renal disease, regardless of which type of hypertensive disorder they have. Women with a history of hypertensive disorders in pregnancy are encouraged to have regular postpartum checkups, especially of renal function.

Key words: hypertensive disorder, renal disease

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Hypertensive disorders in pregnancy (HDPs) affect approximately 2-10% of all pregnancies.[1] They may cause serious perinatal maternal complications and were reported to be 16% of the cause of maternal death in industrialized countries in 2006.[2] Several classification systems have been developed to guide physicians in recognizing and managing serious HDPs.[3-6] HDPs can be classified as gestational hypertension (GH), chronic hypertension, preeclampsia-eclampsia (PE-E), or preeclampsia superimposed on chronic hypertension (PE+SCH).[7]

Most clinical studies focus on PE because of its severity and diversity; only a few studies have focused on other HDPs, especially studies of long-term outcome.[8] Several studies have shown that patients with a history of PE-E have a higher risk of chronic hypertension, cardiovascular disease, and cerebrovascular disease later in life.[9-12] Women with GH were also reported to have a higher risk of subsequent cardiovascular disease than were women without HDPs, but the reported risk is lower than in women with PE.[13-15]

End-stage renal disease (ESRD) is chronic renal failure that necessitates long-term dialysis therapy or renal transplantation, which is a financial and quality-of-life burden. Most patients with chronic kidney disease (CKD) are asymptomatic until uremia syndrome develops. Approximately 2% of women with PE experience acute renal failure, but almost all recover after delivery if they have no history of CKD.[16,17] Vikse et al[18] showed that PE was associated highly with a risk of ESRD after delivery. Having a preterm birth or a low-birthweight baby carries a risk of the development of ESRD. A recent study in Taiwan reported that women with PE-E and GH have a higher risk of ESRD.[19] To our knowledge, no studies have evaluated the risk of ESRD in women with other HDPs. Therefore, the aim of this study was to determine the risk of ESRD in women with various HDPs. All patient information came from Taiwan's nationwide National Health Insurance (NHI) database.

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MATERIALS AND METHODS

Study population

The NHI program began in 1995 and covers 99% of Taiwan's population.[20] All claims data are managed by the National Health Insurance Administration before being transferred to the National Health Research Institutes. We searched a subset of the NHI database for inpatient expenditures by admission codes to identify women who had deliveries between 1998 and 2002. The admission codes are determined by coders based on the physician-determined diagnoses that were recorded in patient charts. Patients who delivered after being diagnosed with ESRD were excluded. Personal identification information was encrypted to secure patient confidentiality. Exemption was obtained from the institutional review board of Chi Mei Medical Center.

The definition of *hypertension* was blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic, or both. *GH* was defined as hypertension that was diagnosed after 20 weeks of gestation and returned to normal limits within 12 weeks after delivery. *Chronic hypertension* was defined as hypertension that was diagnosed either at <20 weeks of gestation or >20 weeks of gestation and persisted for 12 weeks after delivery. PE-E, a syndrome that specifically develops during or shortly after pregnancy, is a complicated HDP. PE is characterized by hypertension and proteinuria that arises at >20 weeks of gestation. *Proteinuria* was defined as daily urine protein ≥0.3 g or ≥1+ on a urinary dipstick reading in a random urine sample. The severity of symptoms and the organs involved in PE are diverse; a new and unexplained seizure in women with PE was diagnosed as eclampsia. PE+SCH is diagnosed when PE develops in pregnant women with chronic hypertension.

According to the diagnosis-related group payment codes, deliveries were classified as natural childbirth (0373A) or cesarean section (0371A or 0373B). All registration files in the NHI database contained 1 primary diagnosis and up to 4 secondary diagnoses based on the codes of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9CM) system. HDP was categorized into 4 types, and each patient was coded for 1 type: PE+SCH (642.7), PE-E (642.4, 642.5, and 642.6), chronic hypertension except secondary to renal disease (642.0 and 642.2), or GH (642.3). Complications of delivery were early delivery (644.2), threatened labor (644.1), and threatened premature labor (644.0). Women with multiple HDPs or other possible causes of ESRD were excluded to clarify the association of a single HDP and ESRD outcome: diabetes mellitus (249 and 250), thrombotic microangiopathy (446.6), hemolytic uremia syndrome (283.11), obstructive uropathy (599.6), systemic lupus erythematosus (710.0), glomerulopathy (580), other nephritis or nephropathy (582 and 583), and hypertension secondary to renal disease that complicated pregnancy, childbirth, and the puerperium (642.1).

The outcome of interest was the occurrence of ESRD. Patients were right-censored on Dec. 31, 2008, or on the date they were issued a catastrophic illness card for ESRD, died, withdrew from the insurance program, or were lost to follow-up evaluation. Patients who underwent hemodialysis for >3 months and were predicted to be hemodialysis-dependent applied for a catastrophic illness card. Patients with ESRD and a catastrophic illness card are subsidized totally by Taiwan's NHI program. Patients were observed for a maximum of 11 years (median, 9 years; interquartile range, 7.09−10.02 years).

Statistical analysis

Pearson's χ^2 test was used to analyze distribution differences in age group, delivery type, number of deliveries, urbanization level, ESRD, death, and complications from delivery between women with and without HDPs. The Student *t* test and the Wilcoxon rank-sum test were used to compare age at first delivery during the study period and time to ESRD, respectively.

The incidence rate of ESRD was calculated as the number of patients with ESRD divided by the total number of person-years. Absolute-risk estimates were calculated as rates per 100,000 person-years of observation. Poisson regression analysis, with total person-years as an offset variable, was used to calculate ESRD incidence-rate ratios and 95% confidence intervals (CIs) for these estimates. In addition, Kaplan-Meier curves were used to describe the proportion of patients who remained ESRD-free, and a log-rank test was used to compare the risk difference between subgroups.

Cox regression analysis was used to determine the relative risk that was adjusted for potential confounding. The validity of the proportional hazards assumption was assessed with the use of Schoenfeld residuals for each variable of interest. SAS software (version 9.2; SAS Institute, Cary, NC) was used for all statistical analyses. Significance was set at a probability value of $< .05$ for women with HDPs only. Because the ratio of women with HDPs to those without is 1:68.28, a probability value of $< .001$ was preferred for this large sample-size study. Kaplan-Meier curves were plotted with the use of Stata software (version 10; StataCorp, College Station, TX).

RESULTS

The study population consisted of 944,474 women who, after giving birth, had been discharged from hospitals in Taiwan; of those women, 13,633 had a history of HDPs, and 930,841 did not. On average, the women with HDPs were older than those without and were more likely to have had a cesarean delivery, to have had only 1 delivery during the study period, and lived in an urban area (Table 1).

During the follow-up period, 0.34% and 0.02% of the women with and without HDPs, respectively, were diagnosed with ESRD. Women with HDPs were more likely than women without to have died or to have had delivery complications. PE-E was the most common HDP (Table 1). Women with HDPs experienced ESRD (median, 3.80 years; interquartile range, 1.94−6.45 years) earlier than those without (median, 5.74 years; interquartile range, 3.62−7.99 years).