OBSTETRICS

Risk factors for new-onset late postpartum preeclampsia in women without a history of preeclampsia

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OBJECTIVE: Risk factors for the development of new-onset late postpartum preeclampsia (LPP) in women without any history of preeclampsia are not known. Because identification of women who are at risk may lead to an earlier diagnosis of disease and improved maternal outcomes, this study identified risk factors (associated patient characteristics) for new-onset LPP.

STUDY DESIGN: A case-control study of 34 women with new-onset LPP and 68 women without new-onset LPP after normal delivery, who were matched on date of delivery, was conducted at Mount Sinai Hospital, New York, NY. Data were collected by chart review. Exact conditional logistic regression identified patient characteristics that were associated with new-onset LPP.

RESULTS: New-onset LPP was associated with age ≥40 years (adjusted odds ratio, 24.83; 95% confidence interval [CI], 1.43—infinity; $P = .03$), black race (adjusted odds ratio, 78.35; 95% CI, 7.25—infinity; $P < .001$), Latino ethnicity (adjusted odds ratio, 19.08; 95% CI, 2.73—infinity; $P = .001$), final pregnancy body mass index of ≥30 kg/m^2 (adjusted odds ratio, 13.38; 95% CI, 1.87—infinity; $P = .01$), and gestational diabetes mellitus (adjusted odds ratio, 72.91; 95% CI, 5.52—infinity; $P < .001$). As predictive tests for new-onset LPP, the sensitivity and specificity of having ≥1 of these characteristics was 100% and 59%, respectively, and the sensitivity and specificity of having ≥2 was 56% and 93%, respectively.

CONCLUSION: Older age, black race, Latino ethnicity, obesity, and a pregnancy complicated by gestational diabetes mellitus all are associated positively with the development of new-onset LPP. Closer observation may be warranted in these populations.

Key words: anticipatory guidance, new-onset late postpartum preeclampsia, postpartum eclampsia, preeclampsia, risk factor

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Preeclampsia is a major cause of maternal and perinatal morbidity and death and affects approximately 5-9% of pregnancies.[1] The onset of preeclampsia can be antepartum, intrapartum, or postpartum.[2,3] New-onset late postpartum preeclampsia (LPP) occurs between 48 hours and 6 weeks after the delivery of a normal pregnancy.[4] Women with preeclampsia during a previous pregnancy are at increased risk of the development of antepartum, intrapartum, and postpartum preeclampsia[5]; thus, clinicians and patients are primed to look for signs of preeclampsia in those women. Although multiple studies have identified risk factors or associated patient characteristics for antepartum and intrapartum preeclampsia in women without any history of preeclampsia,[6] risk factors for new-onset LPP in women without any history of preeclampsia have not been identified.

Studies have shown that early identification and treatment of antepartum preeclampsia may decrease some of the severe maternal, fetal, and neonatal outcomes.[7] Studies have shown that women with LPP in pregnancies that are not complicated by antenatal or intrapartum preeclampsia are at highest risk of the development of eclampsia (a severe outcome) and suggests that women with new-onset LPP should be diagnosed and treated late in their disease.[1] Because women with a history of preeclampsia during any pregnancy are at increased risk of LPP,[5] improved postpartum monitoring of women with any history of preeclampsia may identify some women who are in need of postpartum treatment.

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Who to monitor for new-onset LPP with no history of preeclampsia has not yet been determined.

Because early treatment of antepartum preeclampsia may decrease some severe maternal outcomes,[7] the early treatment of patients with new-onset LPP may also decrease some severe maternal outcomes. The identification of risk factors for new-onset LPP in women without any history of preeclampsia may lead to earlier identification of disease and thus to earlier treatment. To identify those women who are at highest risk of the development of new-onset LPP, we conducted a matched case-control study of women with new-onset LPP without any history of preeclampsia and women without new-onset LPP without any history of preeclampsia.

Materials and Methods

All women who were examined at Mount Sinai Medical Center with the possible diagnosis of LPP are seen routinely by the Maternal Fetal Medicine Division for evaluation and confirmation of the diagnosis. A case of new-onset LPP was defined as any woman who delivered a live-born infant or infants from 2006-2010 at the Mount Sinai Medical Center, who did not have a diagnosis of preeclampsia before labor and delivery in the index pregnancy or in the immediate postpartum period, who did not have a diagnosis of preeclampsia during any previous pregnancy, and who was confirmed by members of the Maternal Fetal Medicine Division to have new-onset LPP after hospital discharge after delivery based the following sign and symptoms from 48 hours to 6 weeks after delivery: (1) multiple blood pressure readings with systolic blood pressure of $\geq$140 mm Hg and/or diastolic blood pressure of $\geq$90 mm Hg or (2) a single recorded systolic blood pressure of $\geq$140 mm Hg or diastolic blood pressure of $\geq$90 mm Hg and $\geq$1 of the following: proteinuria of $\geq$0.3 g protein in a 24-hour specimen, oliguria of $<$500 mL in 24 hours, headache, visual disturbances, pulmonary edema or cyanosis, epigastric or right upper-quadrant pain, impaired liver function, or thrombocytopenia.[8] Control subjects were women who were delivered of a live-born infant or infants at Mount Sinai Medical Center from 2006-2010 and who did not have a diagnosis of preeclampsia at any point in their pregnancy or in the 6 weeks after delivery or in previous pregnancies. Two control subjects were matched to each case-patient based on the date of delivery (day, month, and year) to adjust for seasonality. Patients were excluded if they had a history of any type of preeclampsia in any past pregnancy.

Data were collected by chart review and included demographic data (maternal age, race, ethnicity, clinic vs private setting for antenatal care, marital status, employment status), social habits (cigarette smoking, alcohol use, use of illegal drugs), maternal physical examination at delivery (final pregnancy weight, height, final pregnancy body mass index [BMI]), medical history (asthma, pregestational diabetes mellitus, lupus, chronic hypertension, hypothyroidism, hyperthyroidism, renal disease, medications including any chronic antihypertensive medications), obstetric history (history of preterm labor, history of sexually transmitted disease, previous full-term delivery, previous preterm delivery, nulliparity), characteristics of current pregnancy (gestational diabetes mellitus, use of assisted reproduction, blood pressure before delivery, urinalysis before delivery, mode of delivery, other pregnancy complications), gestational age at delivery, postpartum hospitalization data for case-patients (date of readmission, measured blood pressure, urinalysis, use of antihypertensive medications during hospitalization for new-onset LPP, use of antihypertensive medications at discharge, abnormal liver function, and other laboratory tests [aspartate transaminase, $>$50 IU/L; alanine transaminase, $>$3 IU/L; partial thromboplastin time, $>$35.1 sec; uric acid, $>$7.3mg/dL], and symptoms of preeclampsia that include headache, visual changes, altered mental status, pulmonary edema, peripheral edema, right upper quadrant pain, and seizure).

To identify characteristics associated with new-onset LPP and to maintain the matching of cases and control subjects in the analysis, exact conditional logistic regression was used for univariable and multivariable analysis. With the use of the presence or absence of new-onset LPP as the outcome, an exact conditional regression logistic model for each patient characteristic was built. Characteristics with a probability value of $<$ .20 in individual models were evaluated with the use of forward, backward, and stepwise multivariable exact conditional logistic regression models to identify variables independently that were associated with the outcome. The final model included only those variables that were found to be associated statistically significantly with the outcome.

After characteristics that were associated with new-onset LPP were identified, the crude sensitivity and specificity values for each characteristic were determined; the matching was not taken into account in the calculation of the sensitivity and specificity. The sensitivity and specificity were then determined for a number of associated characteristics.

SAS software (version 9.2; SAS Institute Inc, Cary, NC) was used for the analysis. A probability value of $\leq$ .05 was considered statistically significant. This study was approved by the Mount Sinai School of Medicine Institutional Review Board.

Results

Of 30,476 deliveries at Mount Sinai Hospital during the study period, 1165 deliveries were identified by the International Classification of Diseases, version 9, code of preeclampsia. Of these, 40 deliveries had LPP without any history of preeclampsia during any pregnancy (cumulative incidence, 1.3 per 1000 live-births). Of the 40 case-patients, complete data were available for 34 patients. The case-patients had a mean age of 33.4 $\pm$ 5.1 (SD) years; 38% were black; 32% were Latino, and 21% were white (Table 1). There were approximately an equal number of clinic and private patients. None of the case-patients reported cigarette smoking or alcohol use during pregnancy, and 1 case-patient (3%) reported the use of illegal drugs during pregnancy.

More than 50% of case-patients were diagnosed and readmitted to the hospital