OBSTETRICS

Expectant management of mild preeclampsia versus superimposed preeclampsia up to 37 weeks

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OBJECTIVE: We sought to compare maternal and neonatal outcomes of expectantly managed pregnancies complicated by chronic hypertension with superimposed preeclampsia vs mild preeclampsia up to 37 weeks of gestation.

STUDY DESIGN: This was a multicenter retrospective cohort study of all pregnancies complicated by chronic hypertension with superimposed preeclampsia or mild preeclampsia expectantly managed in the hospital from January 2008 through December 2011. The primary outcomes, adverse maternal and neonatal composite morbidities, were compared between these 2 groups. Frequency differences of maternal adverse outcomes were stratified by gestational age at delivery of <34 and 34-36$^{6/7}$ weeks of gestation.

RESULTS: We found no significant differences in rates of neonatal composite morbidity or latency periods between women with superimposed preeclampsia and mild preeclampsia. Adverse neonatal outcomes were significantly higher at <34 compared to 34-36$^{6/7}$ weeks of gestation (97-98% vs 48-50%) in both cohorts. Maternal adverse composite outcome occurred more frequently in women with superimposed preeclampsia compared to mild preeclampsia (15% vs 5%, $P = .003$; relative risk, 3.0; 95% confidence interval, 1.45–6.29).

CONCLUSION: Women with superimposed preeclampsia have similar neonatal outcomes but more maternal complications than women with preeclampsia without severe features who are expectantly managed <37 weeks.

Key words: expectant management, hypertension, preeclampsia

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Hypertensive disorders are among the most common pregnancy complications. Preeclampsia complicates 3-7% of all pregnancies with a 4-5 times higher incidence in the presence of chronic hypertension.[1-4] These conditions markedly increase the risk of both maternal and neonatal morbidity and mortality.[1,5]

Expectant management with close maternal and fetal surveillance and planned delivery at 37 weeks of gestation is recommended for patients with mild preeclampsia in the absence of other delivery indications.[6-8] The recent American Congress of Obstetricians and Gynecologists (ACOG) Task Force on Hypertension in Pregnancy states that preterm preeclampsia without severe features may be followed expectantly with inpatient or outpatient management.[7] However, many expert authorities recommend hospitalization with a diagnosis of preeclampsia as significant morbidity and mortality are increased even without progression to severe disease.

The broad disease spectrum, especially in the setting of concomitant organ insult, and the challenge of diagnosing preeclampsia in the presence of chronic hypertension has led to a paucity of quality studies regarding optimal

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management. The ACOG Practice Bulletin, addressing chronic hypertension in pregnancy, recommends delivery at 34 weeks of gestation for patients with superimposed preeclampsia.[9] Management and delivery timing in this patient population is based on indirect conclusions from severe preeclampsia studies.[10-12] Patient surveillance and expectant management of severe preeclampsia and chronic hypertension with superimposed preeclampsia at tertiary care institutions are similarly associated with prolonged pregnancy, decreased neonatal intensive care unit stays, and respiratory distress syndrome (RDS) without significant maternal compromise <34 weeks.[10,11,13] Evidence supporting that delivery at 34 weeks of gestation is superior to expectant management until 37 weeks of gestation for superimposed preeclampsia without severe disease is lacking.[7]

Despite the inconsistent recommendations regarding the optimal delivery timing for superimposed preeclampsia diagnosed in the preterm period compared to mild preeclampsia, surprisingly few studies have compared the maternal and fetal outcomes of these 2 conditions.[13,14] Women with chronic hypertension even without subsequent superimposed preeclampsia have increased adverse perinatal outcomes including but not limited to gestational diabetes, fetal growth restriction, cesarean delivery, and worsening hypertension.[1,3,15] Preeclampsia is a risk factor for long-term cardiovascular conditions and it is biologically plausible that superimposed preeclampsia represents further cardiovascular disease and endothelial dysfunction progression, which places women at higher risk of adverse outcomes.[16] Although there are promising studies using imaging and biomarkers to predict preeclampsia and potential disease progression, we still do not fully understand the natural disease process or etiology of preeclampsia, especially superimposed preeclampsia.[17,18]

The purpose of this study is to compare the rates of adverse maternal and neonatal outcomes in patients with mild preeclampsia and superimposed preeclampsia who are managed expectantly in the hospital <37 weeks of gestation. Secondary goal of this study is to analyze outcomes of pregnancies that are stratified between 34-$36^{6/7}$ vs <34 weeks of gestation to gain a better understanding of the natural history of these 2 disease processes. We hypothesize that in the hospital setting with close monitoring, patients with superimposed preeclampsia can be managed safely with similar perinatal risks as patients with mild preeclampsia without a hypertensive history.

Materials and Methods

This was a multicenter retrospective cohort study including 4 tertiary care teaching hospitals. All patients admitted to the University of Cincinnati Medical Center; University of South Alabama Children's and Women's Hospital; Good Samaritan Hospital, Cincinnati; and University of Tennessee College of Medicine, Chattanooga, from January 2008 through December 2011 with a diagnosis of mild preeclampsia or chronic hypertension with superimposed preeclampsia were evaluated for inclusion in this study. The study period was prior to the ACOG Task Force on Hypertension in Pregnancy recommendations for the change in terminology from "mild preeclampsia" to "preeclampsia" and to distinguish superimposed preeclampsia with and without severe features.[7]

This study was approved by the institutional review board at the University of Cincinnati, Cincinnati, OH (#12-03-02-01) and individual institutional review board approval was obtained at all participating centers. *International Classification of Diseases, Ninth Revision* codes and/or antepartum and unit recording systems were used to identify all maternal and associated neonatal charts with the diagnosis of preeclampsia, chronic hypertension, superimposed preeclampsia, and/or preterm birth. Coinvestigators at the individual institutions reviewed all potentially eligible charts, and collected data regarding maternal demographic characteristics, gestational age at diagnosis and delivery, latency period, mode of delivery, indications for delivery, and maternal and neonatal outcomes. Inclusion criteria comprised all singleton pregnancies between $24^{0/7}$ and $36^{6/7}$ weeks of gestation with the diagnosis of mild preeclampsia and chronic hypertension with superimposed preeclampsia that were managed expectantly in the hospital. Exclusion criteria were the diagnosis of severe preeclampsia >$34^{0/7}$ weeks of gestation at the time of admission, preeclampsia requiring delivery immediately after corticosteroids or maternal stabilization, preterm labor or prelabor rupture of membranes on admission, major medical comorbidities not including chronic hypertension, multifetal gestation, congenital anomalies, or other maternal or fetal contraindications to expectant management.

The primary outcomes of the study were composites of maternal and neonatal adverse morbidities. The maternal composite was defined as ≥1 of the following: pulmonary edema, placental abruption, oliguria, and eclampsia. The composite of neonatal morbidities included ≥1 of the following: RDS, intraventricular hemorrhage, necrotizing enterocolitis, bronchopulmonary dysplasia, 5-minute Apgar score of <7, and neonatal death. Secondary outcome was the latency duration from day of admission to delivery. Other maternal morbidities of interest included progression to severe preeclampsia, HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome, abnormal liver enzymes, thrombocytopenia, and maternal death. Additional neonatal complications studied comprised admission to the neonatal intensive care unit and suspected neonatal sepsis. Suspected neonatal sepsis was defined as a neonate receiving antibiotics during a sepsis evaluation regardless of the culture result. All neonatal complications were diagnosed by a board-certified neonatologist. The collected cohort consisted of minimal missing information for primary outcomes of interest, exposure variables, and covariates (<5%).

Patients included in this study were categorized into 2 groups based on the presence or absence of chronic hypertension. Hypertension was defined as

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