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# Assessing progression from mild to severe preeclampsia in expectantly managed preterm parturients

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ABSTRACT

*Objective:* To identify factors associated with shortened latency in expectantly managed women diagnosed with preeclampsia without severe features between 23 0/7 and 35 6/7 weeks' gestation.
*Methods:* This was a retrospective cohort study performed at a large community-based hospital between 2009 and 2014, evaluating all mothers between 23 0/7 and 35 6/7 weeks' gestation with a diagnosis of preeclampsia without severe features. We collected maternal demographics, symptoms, vital signs and laboratory values within six hours of admission. Maternal and neonatal outcomes were stratified by latency period of less than or greater than/equal to seven days (<7 d or ⩾7 d).
*Results:* Overall mean latency was 7.6 ± 12.1 days. When stratifying subjects to <7 d or ⩾7 d latency, neither maternal demographics nor gestational age at diagnosis differed between groups. For subjects with ⩾7 d latency, pregnancy was prolonged by a mean of 24 days compared to the <7 d latency group (34 1/7 vs 30 4/7 weeks GA, P = 0.001). Systolic blood pressure greater than 160 mmHg within the first six hours of hospital presentation correlated with a more than 3-fold risk for requiring delivery within seven days of diagnosis (OR 3.26 95% CI 1.40–7.58).
*Conclusion:* Within our cohort of preterm women admitted with preeclampsia without severe features, elevated systolic blood pressure on admission conveyed significant risk for delivery within seven days.


## 1. Introduction

Preeclampsia is a systemic syndrome characterized by new-onset hypertension and proteinuria occurring in approximately 3–8% of all pregnancies worldwide. Although characterized by poor placental perfusion, the disease may affect any organ system in the body and result in severe maternal and fetal morbidity and mortality. Risk factors for development include extremes of age, obesity, personal or family history of preeclampsia, smoking and certain medical conditions, such as diabetes mellitus, hypertension and renal disease [1,2].

There exists substantial heterogeneity in the timing, presentation and severity of this disease. For instance, a diagnosis of preeclampsia at less than 32 weeks' gestation confers a 20-fold increased risk for maternal mortality, compared to presentation ⩾37 weeks' gestation [1]. However, there is little evidence regarding what factors, if any, predict the temporal progression from mild to severe preeclampsia in women at preterm gestational ages, in whom delivery is commonly delayed to improve neonatal outcomes [1]. Given the varied presentations of the disease, one of the most important clinical challenges providers encounter is ascertaining when the patient with mild preeclampsia will develop severe disease and/or complications. As of yet, no single test has proven predictive of progression from preeclampsia to preeclampsia with severe features [3].

The primary objective of this study was to identify variables that predict the latency period (in days) from time of diagnosis of mild preeclampsia to development of preeclampsia with severe features in women between 23 0/7 and 35 6/7 weeks' gestational age.

## 2. Methods

We conducted a retrospective chart review of all patients admitted to Miller Women's & Children's Hospital Long Beach between January 1, 2009 and December 31, 2014. We identified subjects within our electronic medical record system by using the keywords "preeclampsia", "mild preeclampsia", and "severe preeclampsia". Women with a diagnosis of preeclampsia with

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severe features, or those whose gestational age was greater than 35 6/7 or less than 23 0/7 weeks' gestation were excluded. We chose 35 6/7 weeks' gestation as the upper limit of inclusion in our study in order to detect a meaningful difference – which we considered to be seven days – between subjects managed expectantly and the recommendation for delivery of subjects with mild preeclampsia at 37 weeks' gestation.

Physician admission notes were used to collect demographic information, including age, race, gravidity, parity, gestational age, and number of previous cesarean deliveries. Maternal comorbidities recorded included BMI ⩾ 30, gestational hypertension, chronic hypertension, multifetal gestation, active tobacco use, active drug use, gestational or pre-existing diabetes, preexisting renal disease, hepatic disease, connective tissue disease and a history of preeclampsia or eclampsia. Women with symptoms characteristic of preeclampsia with severe features, such as headache, visual changes, shortness of breath, chest pain, epigastric or right upper quadrant pain, or persistent nausea/vomiting, either in the setting of severe hypertension, abnormal laboratory values and/or persistence beyond the initial six hours of hospital admission, were characterized as having severe features and were thus excluded from study analysis.

The highest systolic and diastolic blood pressures and lowest pulse oximetry recorded within the first twelve hours of presentation to the hospital were noted. Women who exhibited severe-range blood pressures, defined as ⩾160 mmHg systolic or 105 mmHg diastolic, beyond the initial six hours of hospitalization were classified as having severe features and were thus excluded from analysis. We chose to analyze vital signs within the first six hours of admission to allow time for clinical assessment, including repeat blood pressures, laboratory evaluation, response of symptoms to treatment and medical decision making. Additionally, for subjects with mild hypertension, the American College of Obstetricians and Gynecologists' (ACOG) Task Force on Hypertension in Pregnancy defines preeclampsia without severe features as two elevated blood pressures at least than six hours apart.

Laboratory values obtained within six hours of presentation to the hospital were recorded. In cases where laboratory values were repeated within six hours, the most abnormal values of each were used. Proteinuria was defined as 0.3 or greater on urinary spot protein-creatinine ratio or greater than 300 mg on 24-h urine protein collection. Laboratory abnormalities were defined according to the ACOG Task Force on Hypertension in Pregnancy Recommendations [4]. Subjects who met criteria for having severe features based on laboratory abnormalities were excluded from analysis.

Complications were defined as the development of eclampsia, stroke, transient ischemic attack (TIA), posterior reversible encephalopathy syndrome (PRES), pulmonary edema by clinical assessment or SpO2 <90%, need for intubation, myocardial infarction, congestive heart failure, need for inotropic support, hypertension refractory to treatment with labetalol and hydralazine, platelet count <50 k/dL, INR >1.2, disseminated intravascular coagulopathy (DIC), hepatic hematoma formation or hepatic rupture, acute kidney injury, placental abruption, intra-uterine growth restriction less than the 5th percentile, abnormal umbilical artery Doppler studies, fetal demise or maternal death.

One and five-minute Apgar scores, birthweight and number of days spent in the neonatal intensive care unit (NICU) were abstracted from neonates' charts. Neonatal complications included respiratory distress (RDS), necrotizing enterocolitis (NEC), sepsis, pneumonia (PNA), retinopathy (ROP), intracranial hemorrhage (ICH) and death.

Statistical analysis was performed using JMP Software™ (Cary, NC. USA). Chi-square and Fisher Exact Test were performed for categorical variables where appropriate. Student's *T* test was used to evaluate one-way analyses and means used for frequency determination. Outcomes were separated based on latency less than or greater than/equal to 7 days from time of diagnosis to delivery. Multivariate logistic regression was used to control for gestational age when evaluating neonatal outcomes. The decision to stratify women to <7 d or ⩾7 d latency was based on existing literature showing that in expectantly managed preterm women with preeclampsia without severe features, median pregnancy prolongation ranges from 7 to 14 days [5].

## 3. Results

Initial review of our electronic medical record system identified 1029 subjects with a diagnosis of either preeclampsia, mild preeclampsia or severe preeclampsia. After excluding 275 subjects for gestational age and 159 subjects with severe features, 116 subjects remained who met inclusion criteria for preeclampsia without severe features between 23 0/7 and 35 6/7 weeks' gestation. Women averaged 30.2 years of age and were predominantly Hispanic (n = 61, 53.0%). When stratifying subjects by those who delivered before and after seven days' latency, demographic information did not differ between groups, Table 1. The average gestational age at diagnosis and delivery among the overall cohort was 30 4/7 weeks ± 23.7 days and 31 5/7 weeks ± 26.2 days, respectively, with an average latency of 7.6 ± 12.1 days. Of those who remained pregnant longer than seven days, mean latency was 24 days greater compared to those who delivered within the first seven days (34 1/7 weeks GA vs 30 5/7 weeks GA, $P = 0.001$).

A history of preeclampsia in a prior gestation was not associated with longer latency, Table 1. Symptoms present on admission, while affecting as many as 23% of individuals, were not associated with prolonged pregnancy, Table 2. Among vital signs recorded within six hours of admission, systolic blood pressure greater than 160 mmHg was associated with latency shorter than seven days (OR 3.26 95% CI 1.40–7.58), Table 2. The average systolic blood pressure differed significantly between groups (171.0 ± 2.0 mmHg vs 162.3 ± 3.2 mmHg, P = 0.02). While diastolic blood pressure was not associated with shortened latency (OR 2.20 95%

**Table 1**
Demographics.

| | Latency <7 days (n = 84) | Latency ⩾7 days (n = 32) | OR (95% CI) |
|---|---|---|---|
| *Age* | | | |
| <19 | 6.9% (8) | – | 0.94 (0.88–1.0) |
| 20–29 | 27.6% (32) | 9.5% (11) | |
| 30–39 | 31.0% (36) | 15.5% (18) | |
| ⩾40 | 6.0% (7) | 2.6% (3) | |
| *Race/ethnicity* | | | |
| Caucasian | 10.1% (11) | 3.7% (4) | 0.94 (0.56–1.57) |
| Hispanic | 39.5% (43) | 16.5% (18) | |
| Black | 17.4% (19) | 2.8% (3) | |
| Asian | 5.5% (6) | 4.6% (5) | |
| *BMI* | | | |
| 30–34.9 | 18.1% (21) | 7.8% (9) | 0.67 (0.21–2.11) |
| 35–39.9 | 16.4% (19) | 6.9% (8) | |
| ⩾40 | 11.2% (13) | 5.2% (6) | |
| *Maternal comorbidities* | | | |
| Gestational hypertension | 5.2% (6) | 5.2% (6) | 0.33 (0.10–1.12) |
| Chronic hypertension | 21.6% (25) | 5.2% (6) | 1.84 (0.67–5.01) |
| Multiples | 6.9% (8) | 4.3% (5) | 0.57 (0.17–1.89) |
| Tobacco use | 2.6% (3) | 1.7% (2) | 0.56 (0.09–3.49) |
| Drug use | 0.9% (1) | 0.9% (1) | 0.37 (0.02–6.16) |
| Diabetes mellitus | 11.2% (13) | 4.3% (5) | 0.99 (0.32–3.04) |
| Chronic kidney disease | 6.9% (8) | – | – |
| Connective tissue disease | 2.6% (3) | 0.9% (1) | 1.15 (0.12–11.46) |
| History of preeclampsia | 17.2% (20) | 2.6% (3) | 3.02 (0.83–10.98) |

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