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Maternal clinical disease characteristics and maternal and neonatal outcomes in twin and singleton pregnancies with severe preeclampsia

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ABSTRACT

Objective: Based on anecdotal observations, there is concern that severe preeclampsia leads to greater morbidity and mortality for mothers and neonates of twin pregnancies than for mothers and neonates of singleton pregnancies. Because few studies have been done, this study compared maternal disease characteristics and maternal/neonatal clinical outcomes of twin and singleton pregnancies complicated by severe preeclampsia.

Study design: An historical cohort study of patients hospitalized at the Mount Sinai Hospital in New York City, NY, USA, from 2006 to 2010, compared 63 twin and 339 singleton pregnancies complicated by severe preeclampsia via chart review. Women were analyzed in two groups: hospitalized ≤34 weeks gestational age (GA) and hospitalized >34 weeks GA. Univariable analysis (using Chi-square test, Fisher's Exact test, Student's *t*-test, or Wilcoxon Rank-Sum test, as appropriate) then multivariable analysis (using multivariable linear regression or multivariable logistic regression, as appropriate) compared maternal disease characteristics and maternal/neonatal clinical outcomes in twin and singleton pregnancies.

Results: Women with twins were older [mean age 34.9 years (standard deviation (SD) 7.9 years) vs. 29.4 years (SD 7.4 years), *P*-value < .001] and women with singletons had a higher prevalence of chronic hypertension (21% vs. 8%, *P* = .02) and higher prevalence of history of preeclampsia (13% vs. 2%, *P* = .006).

Women with twins were admitted for severe preeclampsia at an earlier gestational age (GA) [median twin 34.9 weeks GA (interquartile range, IQR, 32.7, 36.1) vs. median singleton 37.1 weeks GA (IQR 35.0, 38.9), *P* < .001]. Among women presenting ≤34 weeks GA (27 twins; 108 singletons), women with singletons had a higher mean systolic blood pressure (BP) (181.1 vs. 163.5, *P* < .001), higher mean diastolic BP (108.4 vs. 100.1, *P* = .002), and higher prevalence of headache (56% vs. 30%, *P* = .02). Among women presenting >34 weeks GA (36 twins; 231 singletons), women with singletons had a higher prevalence of headache (54% vs. 28%, *P* = .004).

Conclusion: Mothers and neonates of twin pregnancies complicated by severe preeclampsia do not appear to have greater morbidity and mortality compared to mothers and neonates of singleton pregnancies complicated by severe preeclampsia.

Introduction

Preeclampsia complicates 5–8% of pregnancies [1] and places pregnant women and their fetuses at increased risk of morbidity and mortality. Management of pregnancies with preeclampsia is based on the severity of disease. Women with twin pregnancies are 2–3 times more likely to develop preeclampsia than women with singleton pregnancies [1]. As the incidence of twin gestation increases, the impact of this association is increasingly important [2]. Based on our anecdotal personal interactions with and observations of practicing obstetricians, there is concern that severe preeclampsia leads to greater morbidity and mortality for mothers and neonates of twin pregnancies than for mothers and neonates of singleton pregnancies. However, there are few studies comparing the clinical characteristics of preeclampsia

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disease, and maternal and neonatal outcomes in twin versus singleton pregnancies.

Sibai et al. found that twin gestations complicated by preeclampsia have a higher rate of preterm delivery when compared to singletons [3]. However, it is not known whether this was the result of increased incidence of preterm labor in twins, as 75% of patients were diagnosed with preeclampsia intrapartum or postpartum. While the study found higher rates of preeclampsia in twin gestations, clinical characteristics of preeclampsia disease in twins compared to singletons were not evaluated.

Henry et al. [4] compared clinical characteristics of preeclampsia disease and maternal and neonatal outcomes of singleton and twin pregnancies with severe preeclampsia at the time of delivery, and found similar maternal and neonatal outcomes. However, these findings are of limited utility in predicting patients' clinical courses because the study participants were evaluated at the time of delivery rather than at the time of diagnosis.

We performed an historical cohort study to test the following null hypotheses: in pregnancies complicated by severe preeclampsia, twin pregnancies versus singleton pregnancies are not associated with differences in maternal clinical disease characteristics, and, in pregnancies complicated by severe preeclampsia, twin pregnancies versus singleton pregnancies are not associated with differences in maternal or neonatal outcomes.

Materials and methods

An institutional database was queried to identify all twin and singleton pregnancies complicated by severe preeclampsia delivered at The Mount Sinai Hospital from 2006 to 2010. Severe preeclampsia was defined as having one or more of the following ACOG criteria: systolic blood pressure (BP) ≥160 or diastolic BP ≥110 on two instances at least 6 h apart; symptoms of severe preeclampsia (severe headache, visual changes, epigastric pain); abnormal lab values (transaminase values > twice normal, platelets <100,000, >5 g proteinuria in 24 h); oliguria (<500 mL in 24 h); intrauterine growth restriction (IUGR); or pulmonary edema [1]. The medical records of all potential subjects were reviewed to confirm the diagnosis of severe preeclampsia [1]. Pregnant patients were excluded if they had higher order multiple gestation, presented with intrauterine fetal demise, or had incomplete admission records.

The following clinical information was collected retrospectively from the medical records of pregnant study subjects: demographic data (age, race, insurance, marital status); social habits (cigarette smoking, alcohol use, illicit drug use); past medical history/medical comorbidities (chronic hypertension, asthma, history of sexually transmitted infections, HIV infection, hyperthyroidism, hypothyroidism, lupus, kidney disease); past obstetrical history (gravidity, parity, gestational diabetes, preeclampsia, preterm delivery); comorbidities of current pregnancy (gestational hypertension prior to diagnosis of preeclampsia, gestational diabetes, oligohydramnios, final body mass index, admission in labor or with premature rupture of membranes or preterm premature rupture of membranes); characteristics of current preeclampsia disease (highest blood pressures, oliguria, visual change, pulmonary edema, peripheral edema, epigastric right upper quadrant pain, seizure, headache, development of the syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome), eclampsia, stroke); and current laboratory studies (protein in the urine, hematuria, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, partial thromboplastin time, prothrombin time, creatinine, uric acid, platelet count, and fibrinogen). Maternal management choices, including treatment with antihypertensive medication, treatment with magnesium sulfate, and days from admission to delivery were also noted.

The following clinical information was collected retrospectively from the medical records of newborns of the study mothers: small for gestational age (birth weight < 10th percentile), need for neonatal intensive care unit admission, need for ventilator support, and neonatal mortality.

Statistical analysis

At The Mount Sinai Hospital, patients diagnosed with severe preeclampsia >34 weeks GA are delivered at the time of presentation, whereas patients diagnosed at or prior to 34 weeks may be candidates for expectant management until 34 weeks [5]. Therefore, the analysis was stratified into a ≤34 weeks GA group and >34 week GA group.

Clinical characteristics of disease and maternal and neonatal outcomes were then compared in univariable analysis using Chi-square, Fisher's Exact, *t*-tests or Wilcoxon Rank Sum tests, as appropriate. Clinical characteristics and maternal/neonatal outcomes that were significant in univariable analyses were evaluated further by multivariable analysis; continuous variables were evaluated with multivariable linear regression, and categorical variables were evaluated with multivariable logistic regression.

The multivariable analysis included building a multivariable model for each of the clinical characteristics of preeclampsia disease and maternal/neonatal outcomes found to be significantly different between twins and singletons. Specifically, building a multivariable model used the clinical characteristics of preeclampsia disease or maternal/neonatal outcomes as the outcome variable, twin status as the main exposure, GA at presentation as a necessary covariate, and the differences in maternal demographic data, past medical history/medical comorbidities, prior pregnancy history, and characteristics of current pregnancy that differed between the twins and singleton pregnancies (as described above) as possible confounders. Forward, backward, and stepwise regression was then used to identify the most parsimonious model. When the final multivariable model indicated that twin status was statistically associated with the outcome (*P*-value ≤.05), this was noted and presented in the section 'Results'.

SAS Version 9.3 (Cary, NC) was used for the statistical analysis. A *P*-value of ≤.05 was considered significant. Missing data was

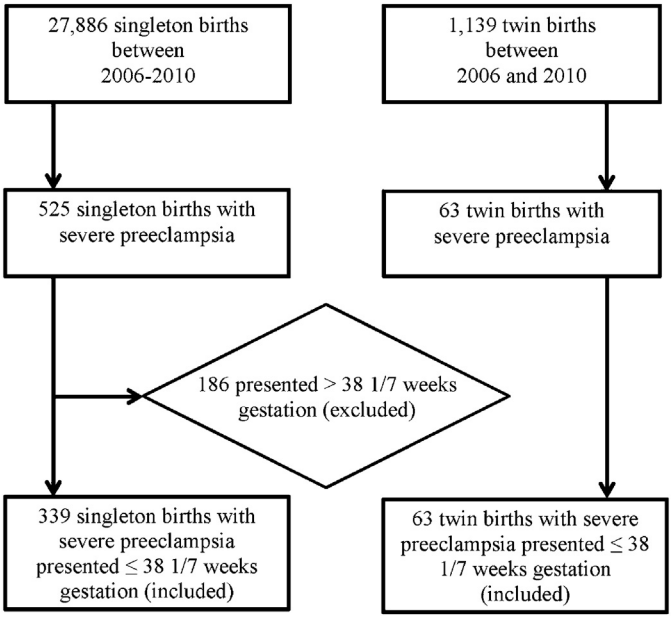

Fig. 1. Selection of study subjects, Mount Sinai Hospital, 2006–2010.