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Adverse Maternal Outcomes Differ between Obese and Nonobese Women with Severe Preeclampsia

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Abstract

Objective—This article evaluates the differences in adverse maternal outcomes related to severe preeclampsia in obese versus nonobese women.

Study Design—Retrospective cohort study and planned secondary analysis of women with severe preeclampsia comparing a composite adverse maternal outcome related to preeclampsia among obese (body mass index [BMI] ≥ 30 kg/m²) and nonobese (BMI < 30 kg/m²) women. The composite outcome was defined as 1 of the following prior to discharge: renal failure, liver abnormality, thrombocytopenia, blood transfusion, pulmonary edema, disseminated intravascular coagulation, stroke, or eclampsia. Multivariable logistic regression was used to control for confounders.

Results—Of the 152 women included, 37.5% were obese and 62.5% were nonobese. The prevalence of the primary outcome was 15.8% with obese women less likely to have the composite outcome compared with nonobese women (7% vs. 21.1%, $p = 0.02$). This remained after adjusting for confounders including maternal age, race, and chronic hypertension (adjusted odds ratio, 0.33 [0.12–0.89], $p = 0.03$). Obese women were, however, more likely to require intravenous antihypertensive medication peripartum compared with nonobese women (49.1% vs. 28.4%, $p = 0.01$).

Conclusion—Obese women with severe preeclampsia may have a different phenotype of severe preeclampsia that is more associated with severe hypertension rather than end-organ damage.

Keywords

obesity; severe preeclampsia; preeclampsia with severe features; adverse maternal outcome; phenotype

Obesity affects more than a third of the reproductive age women with recent reports that approximately 25% of women giving birth in the United States are obese.^{1,2} Obese women

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Conflict of Interest
None.

are at increased risk for adverse pregnancy outcomes including gestational diabetes, venous thromboembolism, and cesarean delivery.^{3–5} Obesity has also been identified as a risk factor for preeclampsia as well as persistent hypertension in the postpartum period.^{6,7} Currently, it is unknown if obese women have a higher risk of morbidity and end-organ damage related to preeclampsia compared with nonobese women. Since obesity and preeclampsia share many similar physiologic and biochemical mechanisms including increased oxidative stress, inflammation, endothelial dysfunction, and vasoconstriction, it is plausible that obese women will be at an increased risk for complications associated with preeclampsia.^{8,9}

Therefore, the objective of this study was to evaluate differences in adverse maternal outcomes related to severe preeclampsia in obese versus nonobese women. We hypothesized that obese women would have an increased rate of adverse maternal outcomes compared with nonobese women.

Methods

A retrospective cohort study of women with severe preeclampsia who delivered at the Hospital of the University of Pennsylvania between July 2011 and February 2013 was performed. The study was approved by the Institutional Review Board. This was a planned secondary analysis of a previously published study on severe preeclampsia that evaluated maternal outcomes based on labor length and mode of delivery. The original study was a retrospective cohort study of women with severe preeclampsia designed to evaluate whether induction, specifically prolonged labor, was associated with adverse maternal outcomes related to preeclampsia and whether cesarean delivery affected the rate of adverse outcomes.¹⁰

Women with severe preeclampsia were identified through the institution's electronic medical and delivery records. The diagnosis was then confirmed by two investigators during chart abstraction. Severe preeclampsia was defined by current recommendations based on the 2013 American College of Obstetricians and Gynecologists' (ACOG) consensus guidelines.¹¹ Women were included in the original study if they were ≥ 34 weeks with a singleton gestation and had a confirmed diagnosis of severe preeclampsia diagnosed before planned cesarean delivery, before induction of labor, or during latent labor. As the original study was evaluating the impact of labor length on adverse outcomes, women diagnosed in active labor or postpartum were excluded. All women from the original study were eligible for this study if they had a recorded body mass index (BMI) before 24 weeks.

We compared obese women (BMI ≥ 30 kg/m²) to nonobese women (BMI < 30 kg/m²) based on the Institute of Medicine guidelines for BMI classification.² BMI was based on height and measured weight at earliest prenatal visit < 24 weeks. The primary outcome of the study was a composite adverse maternal outcome related to severe preeclampsia defined as 1 of the following prior to discharge: renal failure (creatinine ≥ 1.1 g/dL), liver abnormality (liver transaminases > 2 times the normal concentration), thrombocytopenia ($< 100,000$ cells/ μ L), blood transfusion, pulmonary edema (fluid overload requiring diuresis), disseminated

intravascular coagulation (fibrinogen < 250 mg/dL or clinical diagnosis), stroke, eclampsia, and admission to the intensive care unit (ICU).

Secondary outcomes included postpartum hemorrhage (≥ 500 mL blood loss for vaginal delivery or $\geq 1,000$ mL blood loss for cesarean), need for intravenous (IV) antihypertensive medication (during labor and delivery or postpartum), need for an oral antihypertensive medication upon discharge (or additional agent if chronic hypertensive), persistently elevated blood pressure at 6 weeks' postpartum (defined as $\geq 140/90$ and/or need for antihypertensive medication), and neonatal ICU admission (overall and for ≥ 48 hours).

Univariate analyses were performed using chi-square and Fisher's exact tests to compare categorical data. Medians were used to compare nonparametric continuous data. Multivariable logistic regression was used to calculate odds ratio (OR) and adjust for confounders. Covariates were incorporated in the multivariable model if p -value was < 0.2 in univariate analysis. A backward stepwise elimination was then performed to obtain the final model. All data were analyzed using Stata 12.0 (College Station, TX). Statistical significance of $p < 0.05$ was used. There was a fixed sample size based on the parent study.

Results

There were 347 women identified by electronic medical record with severe preeclampsia for the original study which ultimately included 193 women. Of the 193 women included in the parent study, 41 women did not have a BMI recorded before 24 weeks and therefore 152 women met the inclusion criteria for our analysis (►Fig. 1). Of the 152 women included, 57 (37.5%) were obese (BMI ≥ 30 kg/m²) and 95 (62.5%) were non-obese (BMI < 30 kg/m²).

Demographic and clinical information for obese and non-obese groups are shown in ►Table 1. More than 75% of our cohort was African American. Obese women were older and more likely to be multiparous than nonobese women. Chronic hypertension was more prevalent in the obese women and, of the women with chronic hypertension ($n = 6$), none were taking antihypertensive medication prior to admission for preeclampsia. There was no difference in diagnostic criteria for severe preeclampsia between the groups.

The overall prevalence of our primary outcome was 15.8% for the cohort. Obese women were less likely to have the composite adverse maternal outcome compared with nonobese women (7% vs. 21.1%, $p = 0.02$), ►Table 2. This remained significant after controlling for confounders including maternal age, race, and chronic hypertension (adjusted OR, 0.33 [0.12–0.89], $p = 0.03$). The individual components of the primary outcome are listed in ►Table 2. Of note, there were no women that had disseminated intravascular coagulation, stroke, eclampsia, or ICU admission.

►Table 3 summarizes the differences in secondary outcomes between the obese and nonobese groups. Obese women were, however, more likely to require IV antihypertensive medication peripartum compared with nonobese women (49.1% vs. 28.4%, $p = 0.01$). There was no other statistically significant difference in the other secondary outcomes.

Discussion

Among this cohort of women with severe preeclampsia, we unexpectedly found that obese women had a lower risk of our composite adverse maternal outcome compared with nonobese women. Specifically, when adjusting for confounders, obese women were 67% less likely to have the composite adverse maternal outcome. Interestingly, however, while obese women had a lower risk of our composite outcome, they were more likely to require IV antihypertensive treatment during labor and delivery or postpartum. While not statistically significant, there was a trend toward a higher rate of persistent hypertension postpartum for obese women. These findings may represent a different phenotype of preeclampsia for obese and nonobese women.

Different phenotypes of preeclampsia have been previously proposed. Prior studies have characterized these different phenotypes based on several clinical factors.^{12–14} Shahul et al found racial differences in the preeclamptic phenotype. For example, African American women with preeclampsia had an increased rate of maternal complications including acute respiratory distress syndrome, pulmonary edema, and cardiac arrest compared with Caucasian and Hispanic women. Additionally, Hispanic women with preeclampsia had an increased rate of postpartum hemorrhage.¹³ Our population has a large percentage of African American women which may explain our high rate (15%) of adverse outcomes for the cohort. However, there are no differences in the percentage of African American women between our obese and nonobese group and our results remained when adjusting for race. Therefore, race alone cannot completely explain our findings. Lamminpää et al found that advanced maternal age was associated with greater risk of adverse outcome in primiparous women with preeclampsia.¹⁴ In our study, the differences in adverse outcome remained even after adjusting for maternal age.

Our findings support the concept of varying phenotypes for preeclampsia.⁶ Specifically, it appears that obese women are more likely to manifest severe hypertension while nonobese women are more likely to have other systemic manifestations of preeclampsia and end-organ damage. This different phenotype does not equate to obesity representing a “protective” effect on complications of preeclampsia. Rather, obese women with severe preeclampsia may, in fact, have a phenotype of disease characterized by hypertension more so than with other end-organ damage.

The strengths of this study include confirmation of the diagnosis of preeclampsia with severe features by two investigators and the use of current ACOG criteria for diagnosing preeclampsia.¹¹ In addition, the individual components of the composite outcome were clinically meaningful in that, individually they are each associated with maternal morbidity. BMI used in the analysis was recorded < 24 weeks’ gestation, thus limiting the potential confounding of weight gain in pregnancy. The small sample size limits the ability to detect smaller differences in the individual components of the composite outcome as well as secondary outcomes. The study was performed at an urban tertiary care hospital and included a high-risk group of primarily African American women. While this may make our results less generalizable to other populations, these high-risk women are a critical group to focus research on since they are often underrepresented in many studies.

Additional studies examining different phenotypes of preeclampsia in obese women need to be performed to validate our findings. As the prevalence of Class III obesity increases, there may also be an opportunity to investigate more specific subphenotypes within each BMI category leading to more targeted management and monitoring of these individuals. Furthermore, it will be important to follow these women in the long term to determine if the rate of chronic hypertension or other cardiovascular risk factors related to preeclampsia may be, in part, related to the phenotype of preeclampsia that they manifest at the time of disease.

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Fig. 1. Flowchart of patients included in final analysis. Abbreviations: BMI, body mass index.

Table 1

Demographic information for the overall cohort, obese and nonobese groups

Demographic	Nonobese (n = 95)	Obese (n = 57)	p-Value
Race			
African American	72 (75.8)	46 (80.7)	0.78
Caucasian	12 (12.6)	6 (10.5)	
Other	11 (11.6)	5 (8.8)	
Maternal age (y) ^a	24(20.2–30.0)	26.5(23.5–32.7)	0.003
BMI (kg/m ²)			
< 18.5–24.9	57 (60)	-	-
25.0–29.9	38 (40)	-	
30.0–34.9	-	26 (45.6)	
35.0–39.9	-	13 (22.8)	
40	-	18 (31.6)	
Nulliparous	69 (72.6)	22 (38.6)	< 0.001
Gestational age at diagnosis of severe preeclampsia (wk) ^a	37.4(36.1–39)	37.7(36.9–38.6)	0.61
Gestational age at delivery (wk) ^a	37.6(36.4–39.1)	37.9(36.9–38.9)	0.71
Chronic hypertension	1 (1.1)	5 (8.8)	0.03
Diabetes(gestational/pregestational)	7 (7.4)	6 (10.5)	0.5
Other medical condition ^b	18 (19)	17 (29.8)	0.12
Severe preeclampsia diagnosed by:			
Blood pressure alone	58 (61.1)	36 (63.2)	0.67
Symptoms alone	9 (9.5)	7(12.3)	
Laboratory values alone	6(6.3)	5 (8.8)	
Combination	22 (23.2)	9 (15.8)	
Induction of labor	78 (82.1)	49 (86.0)	0.37

Abbreviations: BMI, body mass index; DIC, disseminated intravascular coagulation; ICU, intensive care unit.

Note: Data are presented as *n* (%) unless otherwise indicated. There were no women that had DIC, stroke, eclampsia, ICU admission, or death.^aMedians (interquartile range).^bOther medical condition includes renal disease, history of deep vein thrombosis or pulmonary embolism, epilepsy, history of transplant, and cardiac disease.

Table 2

Differences in the primary outcome in nonobese compared with obese women with severe preeclampsia

Outcome	Nonobese (<i>n</i> = 95)	Obese (<i>n</i> = 57)	<i>p</i> -Value
Composite adverse maternal outcome ^a	20 (21.1)	4(7)	0.02
Renal failure	9 (9.5)	2 (3.5)	0.17
Liver abnormality	7 (7.4)	1 (1.8)	0.13
Thrombocytopenia	9 (9.5)	1 (1.8)	0.06
Blood transfusion	9 (9.5)	1 (1.8)	0.06
Pulmonary edema	0(0)	1 (1.8)	0.20

^aData are reported as *n* (%).

Table 3

Differences in the secondary outcomes in nonobese compared with obese women with severe preeclampsia

Outcome	Nonobese (n = 95)	Obese (n = 57)	p-Value
Cesarean delivery	32 (33.7)	19 (33.3)	0.97
Postpartum hemorrhage	27 (28.4)	18 (31.6)	0.68
Need for intravenous antihypertensive	27 (28.4)	28 (49.1)	0.01
Discharged with oral antihypertensive	22 (23.2)	20 (35.1)	0.11
Persistent hypertension postpartum ^a	8 (14.8)	9 (25.8)	0.18
NICU admission	24 (25.8)	14(25)	0.91
NICU admission > 48 h	21 (22.6)	9 (16.1)	0.34

Abbreviation: NICU, neonatal intensive care unit.

Note: Data are presented as n (%) unless otherwise indicated.

^a
n = 89 for postpartum visit.