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Severe Preterm Preeclampsia: An Examination of Outcomes by Race

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Abstract

Background—Preeclampsia complicates 5–8% of all pregnancies. Previous studies have examined the maternal morbidity and mortality associated with preeclampsia as well as expectant management of preterm severe preeclampsia. However, these studies either did not comment on outcomes by race or were primarily made up of non-black participants.

Objective—To determine if maternal morbidity associated with the expectant management of preterm severe preeclampsia (SPEC) varied by race.

Methods—We performed a retrospective cohort study of women with SPEC diagnosed at <34 weeks between 2008 and 2017 at our institution. SPEC was defined by current ACOG guidelines. The primary outcome was a maternal morbidity composite defined as 1 of the following: HELLP, eclampsia, pulmonary edema, severe renal dysfunction, abruption, maternal ICU admission, venous thromboembolism, blood transfusion, hysterectomy, stroke or death. Secondary outcomes included a composite of neonatal morbidity. Outcomes were compared between self-reported black and non-black women.

Results—275 women were included, 91(33%) were non-black and 184 (67%) were black. Approximately 74% (n=203) underwent expectant management with no difference by race (75.8% non-black vs. 72.8% of black women $P=0.6$). When examining maternal morbidity, 62 women (30.5%) of those expectantly managed developed the composite maternal morbidity outcome with no difference by race (27.5% of non-black vs 32.1% of black women $P=0.5$) even when adjusting for confounders including maternal age, BMI, and parity (aOR 1.02, 95% CI 0.971.35). The median time from diagnosis to delivery (latency time) was 3 days with no difference between the two groups ($p=0.9$) and no difference in neonatal morbidity (60.9% vs. 53%, $p=0.3$).

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Condensation: There were no differences in maternal morbidity between black and non-black women undergoing expectant management of severe preterm preeclampsia.

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Conclusion—Within our population, there were no differences in maternal outcomes between black and non-black women undergoing expectant management of SPEC. More research is needed to determine if the known disparities in maternal morbidity between races are due to factors beyond the antepartum management of SPEC.

Keywords

Black women; Disparities; Expectant management; Maternal morbidity; Non-black women; Preterm severe preeclampsia

Introduction

Preeclampsia is estimated to complicate approximately 5–8% of all pregnancies and is a major cause of maternal morbidity and mortality as well as perinatal complications worldwide.¹ The definitive treatment for preeclampsia is delivery making the diagnosis of preterm preeclampsia an especially challenging circumstance. It requires the balancing of maternal health with the complications associated with prematurity for the neonate. Previous studies have sought to evaluate the maternal morbidity and mortality associated with expectant management of severe preeclampsia to determine the risk of immediate as well as long-term maternal and fetal complications.² These studies were small and primarily composed of non-black women despite the fact that black women are more likely to enter pregnancy with a hypertensive disorder and are more likely to develop a pregnancy related hypertensive disorder including preeclampsia when compared to white women.³

Despite this, there are limited data addressing maternal morbidity and mortality from expectant management of preeclampsia specifically in the black population. For instance, Sibai et al conducted a randomized control trial of women diagnosed with severe preterm preeclampsia between 28 to 32 weeks. In this study had 67% of the participants were black and only half of them (total-34 women) were expectantly managed.⁴ Hall et al represents one of the largest studies of expectant management of preterm SPEC, examining 340 women undergoing expectant management of severe preterm preeclampsia between 24–34 weeks in South Africa. However, these results are from outside of the United States and make no mention of the ethnic make-up of the study participants.⁵ In a prospective observational study conducted in France, of the 239 women undergoing expectant management of preterm SPEC, 63% of the women were white.⁶

Therefore, a more racially diverse evaluation of the outcomes of expectant management are needed to broaden our understanding of the morbidity and mortality of expectant management, focusing on black women, a high risk and underserved patient population. Since both preeclampsia and its associated morbidity differentially impact black women, it is critical to focus research in this population to improve maternal and neonatal outcomes. Therefore, the objective of this study was to determine if maternal morbidity associated with the expectant management of preterm severe preeclampsia (SPEC) varied by race. We hypothesized that outcomes would be worse for black women compared to non-black women.

Materials and Methods

This was a retrospective cohort study of women diagnosed with severe preeclampsia (SPEC) < 34.0 weeks gestational age within the University of Pennsylvania Health system between January 2008 and December 2017. This study received approval from the University of Pennsylvania Institutional Review Board. Women were identified using ICD codes for the diagnosis of SPEC as well as gestational hypertension, with the diagnosis of SPEC confirmed by a trained Obstetrician (JAP). This allowed us to decrease the number of patients missed by incorrect or out dated ICD codes. SPEC was defined by current guidelines based on the 2013 American College of Obstetricians and Gynecologist (ACOG) consensus guidelines. The gestational ages of all pregnancies were determined by ultrasound and last menstrual period according to the ACOG Practice Bulletin *Ultrasound in Pregnancy*.⁸

We compared outcomes for self-reported black women to non-black women. Non-black women were defined as any race other than black. Maternal demographic characteristics as well as their social, medical, and obstetrical history and outcome data were collected via detailed chart abstraction by one reviewer (JAP). All women with the diagnosis of SPEC diagnosed at <34 weeks were eligible for the study. This included women with chronic hypertension diagnosed with super imposed preeclampsia with severe features. Women carrying a pregnancy with a known congenital anomaly were excluded given the reasons for delivery may have been confounded by fetal status and care coordination. As this study focused on expectant management, women who were immediately delivered (defined as delivery within 24 hours of presentation) were excluded from the final analysis although descriptive statistics for this group are presented.

The primary outcome of the study was a composite maternal morbidity defined as 1 of the following outcomes anytime from diagnosis of preeclampsia to 6 weeks postpartum: HELLP (based on ACOG criteria)⁹, eclampsia, pulmonary edema requiring diuresis, severe renal dysfunction, abruption, maternal intensive care unit (ICU) admission, venous thromboembolism, blood transfusion, hysterectomy, stroke or death. The diagnosis of abruption was based on clinical diagnosis and diagnosis of stroke was based on imaging. Severe renal dysfunction was defined as an increase in serum creatinine greater than 1.1 mg/dl or a doubling of baseline creatinine in patients with already known to have renal dysfunction. Pulmonary edema was based on imaging or physical exam and oxygen saturation. This definition includes outcomes and morbidity that can be directly related to preeclampsia itself and has been used in prior preeclampsia related morbidity research.¹⁰

Secondary maternal outcomes evaluated included: latency time to delivery (days), mode of delivery, estimated blood loss and readmission. Secondary neonatal outcomes evaluated included length of stay (days) in neonatal intensive care unit (NICU) and a composite score of neonatal morbidity which included 1 of the following if occurred prior to neonatal discharge: Severe respiratory distress syndrome (defined as intubation and mechanical ventilation for a minimum of 12 hours), culture proven/presumed neonatal sepsis, neonatal blood transfusion, hypoxic ischemic encephalopathy, intraventricular hemorrhage grade 3 or 4, necrotizing enterocolitis, need for head cooling and neonatal demise.

Chi-square and Fisher exact tests were used to compare categorical variables. Wilcoxon Rank Sum was used to compare non-parametric data. Multivariable logistic regression was used to create an adjusted model that including covariates determined to be confounders. A confounder was defined as a covariate that was associated with both the exposure (race) and the outcome (primary composite) with $p < 0.2$. Using a fixed sample size of 275 women, an alpha of 0.05 and a two-sided test, we had 80% power to detect a 1.75-fold difference in maternal morbidity between Black and non-Black women. Data was analyzed using Stata 12.0 (College Station, TX). Statistical significance of $p < 0.05$ was used.

Results

From 2008–2017 there were 275 women identified who were diagnosed with SPEC at < 34 weeks, 91 (33%) were non-black and 184 (67%) were black (Figure 1). Of the non-black women, 63 were white (69.2%), 12 were Hispanic (13.2%) and 16 other (17.6%). This racial and ethnic distribution is comparable to the overall breakdown within the University of Pennsylvania Health system. There was no statistical difference in the median gestational age at diagnosis between non-black and black women (30.1 [28.4–32.1] vs 31.2 weeks [29.3–32.4], $p = 0.08$).

Approximately 74% ($n = 203$) of women were expectantly management with no difference in rate of expectant management by race (75.8% non-black women vs. 72.8% of black women, $p = 0.6$). Among those immediately delivery ($n = 72$), there were 22 non-Black women (24.2%) and 50 black women (27.2%).. The most common reasons women were immediately delivered and not expectantly managed were due to maternal status (67%) including persistent symptoms, persistent severe range blood pressures, abnormal labs and fetal issues (24%) including growth restriction, non-reassuring tracing and fetal demise. These reasons for immediate delivery did not differ by race ($p = 0.2$). There was no statistical difference in the overall composite maternal morbidity between non-black vs. black women who were immediately delivered (40.9% vs 26.0%, $p = 0.2$). Non-black women were more likely to present with laboratory abnormalities than black women (29.7% vs. 19.0%, $p = 0.047$).

Table 1 demonstrates the baseline characteristics of women expectantly managed by race ($n = 69$ non-black, $n = 134$ black women). Non-black women were significantly older than black women and more likely to enter pregnancy with an autoimmune condition although there was no statistical difference in other medical comorbidities including chronic hypertension or diabetes. Black women were more likely to have public insurance and were also more likely to have 5 prenatal visits or less. There was no difference in gestational age at diagnosis or delivery between the two groups.

When examining our primary composite maternal morbidity outcome, among those expectantly managed, 62 women (30.5%) developed the outcome with no difference by race (27.5% of non-black vs 32.1% of black women $p = 0.5$). This held true when restricting the analysis to white vs. black women (25.5% vs. 32.1%, $p = 0.40$). There was also no difference in maternal morbidity outcome among women immediately delivered versus those expectantly managed (30.6 vs. 30.5%, $p = 1.0$). Results continued to be non-significant

when adjusting for confounders including maternal age, BMI, and parity (aOR 1.02, 95% CI 0.97–1.35). Table 2 demonstrates the frequency of the individual components of the primary outcome among those expectantly managed both overall and by race. The most common components of the outcome were renal dysfunction (15.1%) followed by HELLP (9.4%) with no difference by race ($p = 0.80$ and $p = 0.78$ respectively). There was no statistical difference in the individual components of the primary outcome by race although the frequency of adverse outcomes appeared high for Black women throughout.

Eighty-four percent of women were delivered for maternal indications (worsening blood pressures, lab abnormalities, and persistent symptoms), 13% for fetal indications (IUGR, abnormal dopplers and non-reassuring fetal tracing) and 2.5% for other indications. There were no differences in indications for delivery in women undergoing expectant management by race ($p = 0.7$).

The secondary outcomes evaluated are listed in Table 3. There was no difference in cesarean delivery rate ($p = 0.3$). The median time from diagnosis to delivery (latency time) was 3 days (range 1 to 6.2 days) with no difference between the two groups ($p = 0.9$). There was a high rate of the neonatal composite morbidity given the gestational age at delivery although this did not differ between groups ($p = 0.3$). The non-black neonates spent a longer time in the NICU compared to Black neonates (43 days vs. 34 days, $p = 0.05$) however the non-black neonates were also born at a non-significantly earlier median gestational age than the black neonates (30.6 weeks vs. 32.1 weeks, $p = 0.11$).

Discussion

Principal Findings

Our original hypothesis was that black women would have a higher rate of maternal morbidity than non-black women. However, in this retrospective cohort study of women diagnosed with severe preterm preeclampsia undergoing expectant management, we found no differences in maternal outcomes by race with approximately 30% of all women ending up with the primary maternal morbidity composite outcome. Black infants were more likely to have a shorter stay in the NICU when compared to non-black infants although they were delivered 1 week later than non-black neonates. Both groups had a cesarean delivery rate well above average, approaching 80%.

Results

Previous studies that compared racial differences in preeclampsia primarily sought to explore differences in presentation of preeclampsia by race as well as time until delivery. For instance, Goodwin et al conducted a retrospective study of 473 women diagnosed with severe preeclampsia and noted that African American women were more likely to have severe hypertension requiring anti-hypertensive medications while white women were more likely to develop HELLP.¹¹ Similar outcomes were noted in Anseleme et al.¹²

Prior studies did not, however, compare overall maternal morbidity outcomes by race as done in the current study. Our study supports prior literature that demonstrates about a third of women expectantly managed will develop a composite morbidity outcome²; however we

did not identify a difference in morbidity by race. This lack of difference in outcomes between races differs from many other studies demonstrating worse perinatal outcomes for black versus non-black women. Creanga et al demonstrated that African American women had a 5.2 times higher pregnancy-related mortality compared to U.S. born white women.¹³ Additional work has demonstrated African American women to be at higher risk for preeclampsia as well as increased risk of perinatal morbidity and mortality.¹⁴ Our cesarean rate of 80% for this cohort, is comparable to other studies with rates ranging from 71–95%.^{1, 6}

Lastly, prior studies suggested a median time of pregnancy prolongation with expectant management of 5–8 days^{1, 6} which is longer than the 3 days we noted. The exact reason for the difference in latency time from diagnosis is not clear although may be due to differences in delivery indications. Regardless, a three day time period in a preterm gestation is still significant in allowing for interventions such as betamethasone administration.

Clinical Implications

Given the known disparities in many perinatal outcomes between black and non-black women, it was critical to evaluate differences in outcomes among this high risk group of women - African American women with severe preeclampsia. There are many hypotheses as to why our study results may not have found differences in preterm SPEC outcomes by race. In general, there is a lack of understanding as to why perinatal outcomes differ by race and whether this difference is the result of antepartum, intrapartum or postpartum care. While there appears to be differences in access to care, there may also be differences in recognition and management of disease based on race. Inpatient expectant management of preterm SPEC may be a unique situation for two reasons. One is that all women are admitted for expectant management, potentially decreasing the social or financial barriers to obtaining and receiving follow-up outpatient care. Moreover, as a function of inpatient admission, the patients all receive close monitoring and expeditious delivery if needed. Another is the fact that the management of preterm SPEC is evidenced based with routine guidelines recommended by ACOG⁷ including which patients to expectantly manage and when to deliver and therefore this condition has a more standard and protocolized approach to management compared to many other aspects of obstetrical care. It is perhaps the standardization of care that occurs, regardless of race, that helps eliminates disparities in care and outcomes with expectant management of preterm SPEC. In addition, our study looked at the period from delivery to six weeks postpartum and thus was not able to capture delays in diagnosis or admission prior to admission to our health system or postpartum complications if patients presented to other institutions. As a tertiary care center, our health system often receives transfers from facilities in the region and transfers people back to their original location of prenatal care after their deliveries, thus limiting our ability to capture delays in diagnosis prior to admission or after being discharged from our care.

Strengths and Limitations

A strength of this study is the inclusion of patients from two hospitals within our medical system. One hospital is an urban academic medical center with a large underserved population while the other hospital is an academic community hospital serving a larger

portion of privately insured patient. This increases the generalizability of our findings. However, our medical system routinely cares for a large proportion of black women (more than 60% of our population) and it is therefore not known how this may influence our overall outcomes - could this be another factor leading to equal outcomes for the black women in our population? Another strength is the components of the composite outcomes for maternal and neonatal morbidity were composed of clinically significant outcomes. We had a fixed sample size limited by the number of women with severe preterm preeclampsia available within our institution during the 10-year time-frame evaluated. While we were powered to see a 1.75-fold difference in outcomes between Black and non-Black women, smaller differences than this would still be clinically meaningful and therefore we are limited by the small sample size. With that said, this is still one of the largest studies that is able to compare racial differences in women expectantly managed with severe preterm preeclampsia since more than two-thirds of our population was black. Lastly, the number on non-Black, non-Caucasian races were small, limiting our ability to conduct specific analyses among other races, including for example, Hispanic.

Conclusion

The Institute of Medicine's document entitled *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care* notes that clinical encounters can be fraught with stereotyping and biases and that the structure of healthcare systems themselves can contribute to unequal treatment and thus unequal outcomes.¹⁵ Our study raises an interesting question as to whether standardization of care may help to remove an element of implicit bias that can be leading to differences in outcomes. Further exploration into how issues of access, bias and engagement with the healthcare systems as well as medical management of pregnancy complications contribute to disparities in maternal morbidity and mortality is needed.

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AJOG at a Glance

- A. Why was this study conducted?** To determine if maternal morbidity associated with the expectant management of preterm severe preeclampsia (SPEC) varied by race.
- B. What are the key findings?** There were no differences in maternal morbidity between black and non-black women undergoing expectant management of severe preterm preeclampsia.
- C. What does this study add to what is already known?** Previous smaller studies have sought to demonstrate the complications associated with preeclampsia but have not commented on whether morbidity is affected by race.

Highlights

- There was no difference by race in the latency to delivery in those undergoing expectant management of severe preterm preeclampsia.
- There was no difference in maternal morbidity composite in black women as compared to non-black women diagnosed with preterm severe preeclampsia.
- The cesarean rate was approximately 80% in those diagnosed with preterm severe preeclampsia.

Figure 1:
Flow diagram of women included in the study

Table 1.**Maternal Characteristics Between Groups**

	Expectantly managed, non-black N= 69	Expectantly managed, black N= 134	p-value
Maternal age (years) ^a	33.0[29.7–37.2]	29.8 [24.1–34.4]	<0.001
Obese (BMI ≥ 30 kg/m ²)	17 (24.6)	78 (58.2)	<0.001
Nulliparous	50 (72.5)	61(45.5)	<0.001
Autoimmune disease	8 (11.6)	5 (3.7)	0.03
Chronic Hypertension	17 (24.6)	51 (38.1)	0.06
Pre-gestational diabetes	4 (5.8)	12 (9.0)	0.4
Pre-existing renal dysfunction	3 (4.4)	6 (4.5)	1.0
Gestational diabetes	5 (7.4)	5 (3.8)	0.3
Public insurance	12 (17.4)	91(67.9)	0.001
Number prenatal care ^b	6.5 (2.2)	5.7 (2.6)	0.04
Gestational age at diagnosis (weeks) ^a	30.1 [28.4–32.1]	31.2 [29.3–32.4]	0.08
Gestational age at delivery (weeks) ^a	30.6 [28.6–32.5]	32.1 [30–33.1]	.11

Data are presented as n (%) unless otherwise indicated

^aMedian [inter-quartile range]

^bMean (Standard Deviation)

Table 2.

Individual components of the primary outcome among women expectantly managed

Component of the primary outcome	Total n (%)	Non-black N=69	Black N=134	p-value
Overall composite	62(30.5)	19(27.5)	43(32.1)	p=0.51
Renal dysfunction	30(15.1)	11(15.9)	19 (14.2)	p=0.80
HELLP	19 (9.4)	7(10.1)	12 (8.96)	p= 0.78
Abruption	13 (7.3)	5(6.0)	8(61.5)	p=0.74
Transfusion	12(5.9)	4(5.8)	8 (5.97)	p=0.96
Intensive care unit admission	6(3.0)	2(2.9)	4 (2.99)	p=0.97
Pulmonary edema	5(2.5)	0 (0)	5 (3.8)	p=0.10
Venous thromboembolism	4(2.0)	1(1.5)	3 (2.2)	p=0.70
Eclampsia	2(1.0)	0 (0)	2 (1.5)	p=0.31
Hysterectomy	1(0.5)	0(0)	1(0.75)	p= 0.47

HELLP: Hemolysis Elevated Liver Function Low Platelets

Table 3.

Secondary Outcomes among women expectantly managed

	Expectantly managed, non-black N= 69	Expectantly managed, black N=134	p-value
Cesarean rate ^a	57 (82.6)	103 (76.9)	0.3
Latency to delivery (days) ^b	3 [1–6]	3[1–6]	0.9
Neonatal composite ^a	42 (60.9)	71 (53.0)	0.3
Days in NICU ^b	43 [24–70]	34[22–56]	0.048

^aData presented as n (%)^bData presented as median [Inter-quartile range]

NICU: neonatal intensive care unit