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Racial Disparities in Comorbidities, Complications, and Maternal and Fetal Outcomes in Women with Preeclampsia/Eclampsia

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Abstract

Objective—The mechanisms leading to worse outcomes in African-American (AA) women with preeclampsia/eclampsia remain unclear. Our objective was to identify racial differences in maternal comorbidities, peripartum characteristics, and maternal and fetal outcomes.

Methods/Results—When compared to white women with preeclampsia/eclampsia, AA women had an increased unadjusted risk of inpatient maternal mortality (OR 3.70, 95% CI: 2.19-6.24). After adjustment for covariates, in-hospital mortality for AA women remained higher than that for white women (OR 2.85, 95% CI: 1.38-5.53), while, the adjusted risk of death among Hispanic women did not differ from that for white women. We also found an increased risk of intrauterine fetal death (IUFD) among AA women. When compared to white women with preeclampsia, AA women had an increased unadjusted odds of IUFD (OR 2.78, 95% CI: 2.49-3.11), which remained significant after adjustment for covariates (adjusted OR 2.45, 95% CI: 2.14-2.82). In contrast, IUFD among Hispanic women did not differ from that for white women after adjusting for covariates.

Conclusions and Relevance—Our data suggest that African American women are more likely to have risk factors for preeclampsia and more likely to suffer an adverse outcome during peripartum care. Future research should examine whether controlling co-morbidities and other risk factors will help to alleviate racial disparities in outcomes in this cohort of women.

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None.

Keywords

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Introduction

African Americans (AA) experience a threefold higher risk of mortality from pregnancy related complications when compared to white women¹⁻⁴. The mortality rate for AA and white mothers is 38.9 and 12.0 per 100,000 live births⁴ and has remained unchanged for the last 50 years with approximately 44% of these deaths deemed preventable⁵

Hypertensive disorders of pregnancy, including preeclampsia/eclampsia, are among the causes of maternal death deemed most preventable by the National Partnership for Maternal Safety.⁶ In AA women with hypertensive disorders of pregnancy, previous studies have demonstrated higher complication rates and mortality even after controlling for socioeconomic differences^{2, 7, 8}. Higher case fatality rates from preeclampsia/eclampsia in African-American women contribute to these observed mortality differences². However, no large, population based studies have examined why these differences in maternal and fetal outcomes exist. We hypothesized that AA women with preeclampsia/eclampsia were more likely to suffer higher rates of severe maternal comorbidities and complications including congestive heart failure (CHF), cardiac arrest, stroke, etc. which may then contribute to worsened peripartum maternal and fetal outcomes. Identifying severe maternal comorbidities may help clinicians devise strategies for improving both maternal and fetal outcomes in this patient population.

In this study, we used data from the National Inpatient Sample to examine racial differences in the incidence of preeclampsia/eclampsia in the United States. We then compared differences between white, African American (AA), and Hispanic women with respect to maternal comorbidities, characteristics of pregnancy and delivery, complications and maternal and fetal mortality, in parturients with preeclampsia and eclampsia.

Methods

Data Source

We performed a retrospective cohort analysis using data from the National Inpatient Sample (NIS) from 2004 to 2012. The NIS database provides discharge data on approximately eight million hospital stays annually, is maintained by the Healthcare Utilization Project (HCUP) of the Agency for Healthcare Quality and Research, and is the largest inpatient care database in the United States⁹. The NIS randomly samples 20% of all discharges from all HCUP hospitals (N= 4,378 in 2012). National estimates are obtained by weighting NIS data to provide data estimates for 95% of all inpatient hospitalization in the United States. The NIS dataset includes demographic information, comorbidities, hospital characteristics, procedures performed, inpatient mortality, and disposition.⁹ Hospitals can also be stratified based on region, ownership/control (profit/nonprofit), teaching status, bed size and location (urban/rural). Because the NIS has no data elements that identify individual patients, the

Committee on Clinical Investigations at both Beth Israel Deaconess Medical Center and the University of Chicago declared this study exempt.

Data in the NIS is validated using both internal and external quality assessments. External validation was excellent when compared against the American Hospital Association Annual Survey Database, the National Hospital Discharge Survey from the National Center for Health Statistics and the MedPAR Inpatient Data from the Centers of Medicare and Medicaid Services¹⁰.

Study Population

The study population included all patients in the NIS with a diagnosis of preeclampsia/eclampsia from 2004 through 2012, as identified by the presence of *International Classification of Diseases*, Ninth Revision (ICD-9-CM) codes on discharge.

Exposure, Outcome and Covariates

The exposure of interest was the patient's race (white, AA, or Hispanic). NIS defines race as white, black, Hispanic, Asian or Pacific Islander, Native American and other. The primary outcome was inpatient mortality during hospitalization. IUFD was defined as fetal demise during hospitalization. Potential confounders were identified and adjusted for in our final analysis.

Covariates were identified based upon known risk factors for preeclampsia that include parity, multiple gestation, diabetes (including gestational diabetes), obesity and preexisting hypertension

To account for potential confounding due to known risk factors for preeclampsia we adjusted for age, characteristics of pregnancy (parity, preterm labor), delivery type (Caesarean section versus vaginal), and maternal characteristics (diabetes, gestational diabetes, obesity). To adjust for socioeconomic status we utilized median household income of residents in the patient's zip code, payer type (Medicare, Medicaid, private insurance, self-pay, no charge and other), region and hospital type.

Missing data

In our study cohort, race was missing in 18.36% of patient admissions. We used two approaches to account for these missing data. We first performed the analysis only on patients in our cohort who had complete case information (complete case analysis). We then performed multiple imputation to generate missing values for race using a weighted sequential hot deck method which does not place any restrictions on missing data patterns to create five complete datasets¹¹. Pooled values were then utilized to calculate race-specific outcomes. This multiple imputation approach is recommended by HCUP to overcome any inherent biases in the complete case analysis approach¹².

Statistical Analysis

All analyses were performed using SAS 9.3 (SAS Institute, Cary, NC) and SUDAAN 10.0 (Research Triangle Institute, Research Triangle Park, NC). For all analyses, weighted

estimates were used to adjust for design effects of the sampling. Categorical variables were presented as frequencies or proportions and compared using the chi-square test. An unadjusted logistic regression model was used to estimate the risk of inpatient mortality among patients with preeclampsia/eclampsia relative to race. We then used a multivariate adjusted model, with terms for patient age, median household income, region, hospital type and region, mode of delivery, parity, diabetes, year and payer type. To account for in-hospital clustering we used generalized estimating equations with robust variance estimates. All tests were two sided and p-values <0.05 were considered statistically significant.

Results

Demographics and Patient Characteristics

Demographics, clinical characteristics, and comorbidities of our study cohort are presented in Table 1. We identified 1,175,046 weighted patient discharges with preeclampsia/eclampsia. The incidence of preeclampsia was 6.04% in African American women, compared to 2.58% in Hispanic women and 3.75% among white women ($p < 0.0001$). AA women with preeclampsia were younger than white women and more likely to reside in areas in the lowest quartile for median income.

Patient Comorbidities

When compared to white women, AA women with preeclampsia had a higher rate of hypertension, diabetes, obesity, and acute renal failure (Table 1).

Pregnancy, delivery characteristics and obstetrical complications

AA women with preeclampsia/eclampsia were more likely to be multiparous, to have a placental abruption, and to have undergone a delivery by cesarean section than white women (Table 1). Although AA women with preeclampsia/eclampsia had similar rates of postpartum hemorrhage than white women, Hispanic women had higher rates of postpartum hemorrhage than both African American and white women (Table 2).

Peripartum Complications

The incidence of peripartum complications are listed in Table 2. When compared to white women, AA women with preeclampsia/eclampsia had a higher likelihood of severe maternal complications including cardiac arrest, acute respiratory distress syndrome (ARDS), pulmonary edema, pulmonary embolism, congestive heart failure and peripartum cardiomyopathy, and mechanical ventilation. (Figure 1).

Inpatient Mortality

When compared to white women with preeclampsia/eclampsia, AA women had an increased unadjusted risk of inpatient maternal mortality (OR 3.70, 95% CI: 2.19-6.24). After adjustment for covariates, in-hospital mortality for AA women remained higher than that for white women (OR 2.85, 95% CI: 1.38-5.53). In contrast, the unadjusted and adjusted risk of death among Hispanic women did not differ from that for white women (unadjusted OR 1.81, 95% CI: 0.98-3.36; adjusted OR 1.44, 95% CI: 0.74-2.79). (Table 3). Similar mortality

differences between AA and white women were observed after multiple imputation for both unadjusted (OR 3.93, 95% CI: 2.41-6.54) and adjusted analyses (OR 2.88, 95% CI: 1.63-5.10).

Intrauterine Fetal Death (IUFD)

We also found an increased risk of intrauterine fetal death (IUFD) among AA women. When compared to white women with preeclampsia, AA women had an increased unadjusted odds of IUFD (OR 2.78, 95% CI: 2.49-3.11), which remained significant after adjustment for covariates (adjusted OR 2.45, 95% CI: 2.14-2.82). In contrast, IUFD among Hispanic women did not differ from that for white women (adjusted OR 0.96, 95% CI: 0.82- 1.13). (Table 3)

Discussion

Using the National Inpatient Sample, we found racial disparities in severe maternal morbidities and peripartum characteristics among preeclamptic women. Our data are consistent with previously published observations that AA women develop preeclampsia at higher rates than their white counterparts^{2, 7, 8}. In addition, we found that AA women with preeclampsia had higher rates of maternal and obstetric complications, and experienced higher unadjusted and adjusted odds of mortality when compared to white women with preeclampsia/eclampsia. Finally, we observed that AA women had higher unadjusted and adjusted odds of IUFD when compared to white women.

Several explanations are possible for our data. AA women had higher odds of severe maternal complications, which may have resulted in the observed differences in maternal and fetal outcomes. Previous work has demonstrated an increased prevalence of cardiovascular disease¹³⁻¹⁸ among AA women when compared to white women, and also higher mortality rates for congestive heart failure^{14, 19}, coronary artery disease^{13, 15, 18, 20}, hypertension^{20, 21} and stroke^{15, 18, 20}. The explanation for these previously noted disparities in cardiovascular disease and death rates are incompletely understood but may include genetic differences, and disparities in socioeconomic status, limited access to health care, and limited awareness among practitioners of outcome disparities^{16, 18, 20, 22-25}.

In our analysis, we demonstrate a previously unreported higher incidence of comorbidities among AA women that may be risk factors for preeclampsia/eclampsia, including hypertension, diabetes, obesity, acute renal failure and chronic renal failure. It is possible that more aggressive treatment of these underlying comorbidities may improve outcomes for AA women with preeclampsia. Similar racial disparities in adverse outcomes have been observed for many of these individual complications in non-pregnant patients.^{20, 26-29} Recent evidence suggests it may be possible to eliminate some racial outcome disparities by medical treatment of certain risk factors (e.g., blood pressure, cholesterol, glycosylated hemoglobin).^{18, 30-32}

We found that the increased likelihood of both maternal and fetal mortality among African American parturients with preeclampsia persisted despite adjustment for socioeconomic and insurance status (SES). This finding suggests that although disparities in socioeconomic

status may contribute to racial disparities in outcome, as has been noted in other diseases, other factors may also play a role^{13, 15, 19, 22, 25, 27, 29}.

Hypertension is a major contributor to the etiology of many of maternal complications that we observed, including CHF, pulmonary edema, and stroke³³⁻³⁶. Previous work has demonstrated that AA women not only develop more severe hypertension earlier than white women, but also have higher rates of mortality from hypertension-related end organ damage such as CHF and stroke when compared to other ethnic racial groups³⁷⁻³⁹. Whether treating maternal hypertension more aggressively in AA women will improve outcomes is unclear. In a recent trial comparing tight (diastolic blood pressure <85mmHg) versus less tight control (DBP<100 mmHg) of blood pressure in mothers with non-proteinuric, preexisting or gestational hypertension, Magee et al demonstrated that although tight control of blood pressure significantly decreased the incidence of severe hypertension (>160/110 mmHg), maternal outcomes or neonatal outcomes did not differ between groups, and progression to preeclampsia occurred at equal rates between groups⁴⁰. While that trial did enroll AA women, it was not powered to answer the question of whether AA women with hypertension will have improved outcomes with tighter control of blood pressure in pregnancy.

Our study contributes to the existing body of literature on outcomes in AA women with preeclampsia. Work in the last decade has demonstrated increased mortality among AA women with preeclampsia.^{2, 7, 8} Our data, which draws from a much larger sample, reinforces the presence of racial disparities in outcome and suggests that such disparities may be larger than previously thought. We also provide evidence of an increased incidence of associated comorbidities and severe complications that may account for the increased mortality.

A primary strength of our study was our use of a large, nationally representative sample of patients from the NIS from 2004 to 2012. However, our study also has several limitations. Despite a prevalence of preeclampsia similar to that in previous studies, we were unable to independently verify coding accuracy for race, socioeconomic variables, comorbidities, and outcomes. Also, because the NIS is an administrative database and because of our retrospective study design, we could not verify causal links between race, comorbidities and outcomes. For example, NIS data are unable to determine the time course between disease onset and mortality. Finally, the NIS is only a 20% sample of all hospital discharges, and may not be fully representative of current trends in preeclampsia/eclampsia care.

In conclusion, we have identified racial disparities in maternal and fetal outcomes among women with preeclampsia. Our data suggest that African American women are more likely to have comorbidities associated with preeclampsia, and more likely to suffer an adverse outcome during peripartum care. Future research should examine whether better medical management of comorbidities and treatment of peripartum complications will reduce racial disparities in preeclampsia/eclampsia outcomes.

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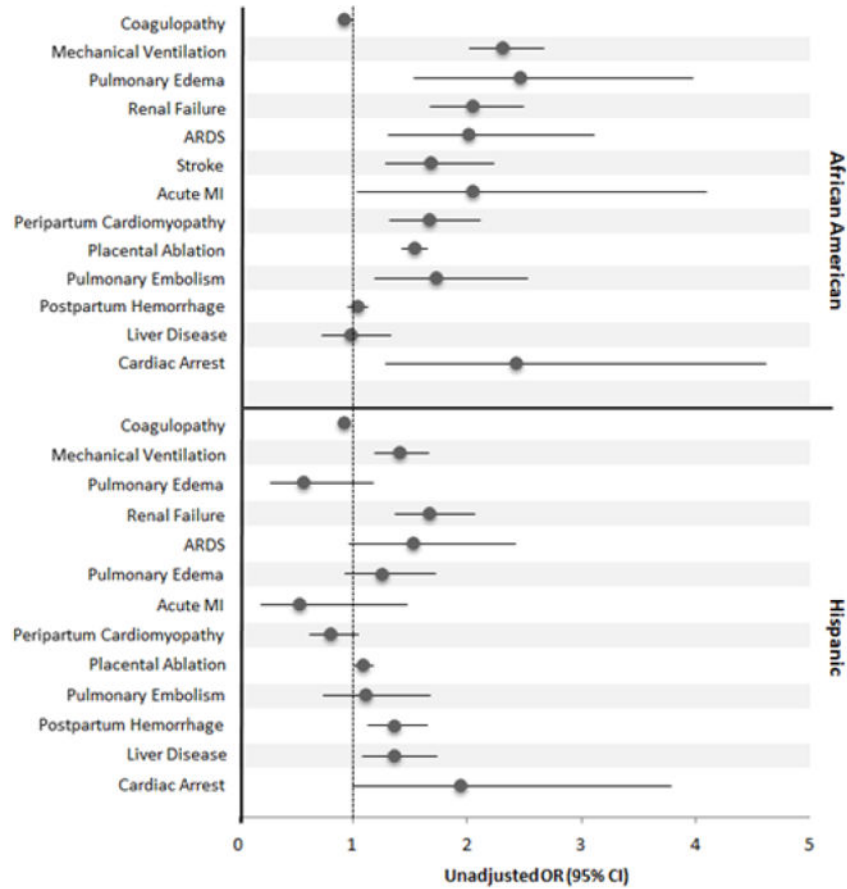


Figure 1. Odds ratios for severe maternal complications in African American and Hispanic women with preeclampsia. African American women were significantly more likely than white women to need mechanical ventilation, develop pulmonary edema, renal failure, ARDS, stroke, acute MI, peripartum cardiomyopathy, placental ablation, pulmonary embolism, or cardiac arrest.

Table 1

Patient Characteristics at Presentation

	Weighted N (%)			P-Value
	White	Black	Hispanic	
No. of Patients	568124 (3.75)	235007 (6.04)	268014 (2.58)	<0.0001
Age (years)				
10 – 19	28135 (5.48)	25115 (11.86)	26767 (11.07)	
20 – 29	256729 (49.99)	111925 (52.88)	123190 (50.97)	<0.0001
30 – 39	203769 (39.68)	65958 (31.16)	81266 (33.62)	
40 – 49	24913 (4.85)	8675 (4.10)	10472 (4.33)	
Median Household Income for Patient's Zip code (percentile)				
0 - 25th	127504 (22.42)	116237 (49.94)	106755 (40.22)	
26th - 50th	148532 (26.12)	51382 (22.08)	65418 (24.65)	<0.0001
51st - 75th	151746 (26.68)	39509 (16.97)	55926 (21.07)	
76th - 100 th	140973 (24.79)	25627 (11.01)	37304 (14.06)	
Primary Expected Payer				
Medicare	4583 (0.80)	3503 (1.46)	1395 (0.51)	
Medicaid	175778 (30.50)	147173 (61.51)	174834 (64.03)	
Private Insurance	367865 (63.83)	76687 (32.05)	73572 (26.94)	<0.0001
Self-pay	8885 (1.54)	6561 (2.74)	17016 (6.23)	
No Charge	713 (0.12)	680 (0.28)	1796 (0.66)	
Other	18463 (3.20)	4667 (1.95)	4451 (1.63)	
Hospital Characteristics				
Hospital Region				
Northeast	108309 (18.77)	49173 (20.49)	36063 (13.20)	
Midwest	117231 (20.31)	33122 (13.80)	11394 (4.17)	<0.0001
South	236670 (41.01)	139447 (58.12)	119230 (43.63)	
West	114921 (19.91)	18200 (7.59)	106616 (39.01)	
Patient Comorbidities				
Hypertension	53826 (9.33)	40040 (16.69)	23319 (8.53)	<0.0001

	Weighted N (%)			P-Value
	White	Black	Hispanic	
Obesity	47199 (8.18)	28619 (11.93)	20965 (7.67)	<0.0001
Diabetes Without Chronic Complications	15385 (2.67)	8374 (3.49)	9518 (3.48)	<0.0001
Diabetes With Chronic Complications	2828 (0.49)	1498 (0.62)	1257 (0.46)	<0.0001
Renal Failure	1252 (0.22)	1054 (0.44)	994 (0.36)	<0.0001
Liver Disease	1039 (0.18)	415 (0.17)	673 (0.25)	<0.0001
<i>Pregnancy and Delivery Characteristics</i>				
Multiple Gestation	39724 (6.88)	10433 (4.35)	9635 (3.53)	<0.0001
Multiparity	2783 (0.48)	3426 (1.43)	3460 (1.27)	<0.0001
Cesarean Delivery	324787 (26.28)	137240 (57.20)	144268 (52.79)	0.0001

Table 2

Complications

	<i>Weighted N (%)</i>			P-Value
	White	Black	Hispanic	
Patient Complications				
Acute Respiratory Distress Syndrome (ARDS)	200 (0.03)	166 (0.07)	145 (0.05)	0.08
Pulmonary Edema	162 (0.03)	166 (0.07)	44 (0.02)	0.0005
Pulmonary Embolism	331 (0.06)	235 (0.10)	174 (0.06)	0.10
Congestive Heart Failure	1752 (0.30)	1275 (0.53)	728 (0.27)	<0.0001
Peripartum Cardiomyopathy	1020 (0.18)	701 (0.29)	389 (0.14)	0.0003
Mechanical Ventilation	2070 (0.36)	1972 (0.82)	1380 (0.50)	<0.0001
Coagulopathy	13675 (2.37)	5325 (2.22)	5614 (2.05)	0.01
Stroke	573 (0.10)	397 (0.17)	343 (0.13)	0.03
Cardiac Arrest	85 (0.01)	85 (0.04)	78 (0.03)	0.0001
Died	123 (0.02)	189 (0.08)	105 (0.04)	0.001
Obstetrical Complications				
Intrauterine Fetal Death	3137 (0.54)	3591 (1.50)	1811 (0.66)	<0.0001
Placental Abruption	12814 (2.22)	7983 (3.33)	6605 (2.42)	<0.0001
Postpartum Hemorrhage	32662 (5.66)	13765 (5.74)	20696 (7.57)	<0.0001

Table 3

Adjusted and Unadjusted Associations between Race and Complications for Patients with Preeclampsia/Eclampsia

	<i>Race</i>		
	White	Black	Hispanic
Unadjusted OR (95% CI)			
Maternal Mortality	1.0 [Reference]	3.70 [2.19, 6.24]	1.81 [0.98, 3.36]
Intrauterine Fetal Death	1.0 [Reference]	2.78 [2.49, 3.11]	1.22 [1.08, 1.39]
Adjusted OR* (95% CI)			
Maternal Mortality**	1.0 [Reference]	<u>2.85 [1.38, 5.53]</u>	<u>1.44 [0.74, 2.79]</u>
Intrauterine Fetal Death [‡]	1.0 [Reference]	2.45 [2.14, 2.82]	0.96 [0.82, 1.13]

** Adjusted for age group, median household income, hospital region, teaching status, mode of delivery, multiparity, diabetes (with and without complications), year, preexisting hypertension, obesity and payer type

[‡] Adjusted for age group, median household income, hospital region, teaching status, mode of delivery, multiparity, diabetes (with and without complications), year, obesity and payer type