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Pre-eclampsia in American Indians/Alaska Natives and Whites: The Significance of Body Mass Index

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Abstract

Introduction—The prevalence of pre-eclampsia, a major cause of maternal morbidity, varies by race, being greater in African Americans, and lower in Asians and Hispanics than in White women. Little is known about its prevalence in American Indians/Alaska Natives (AI/ANs). We estimated pre-eclampsia risk in AI/ANs compared to Whites, with consideration of the potential effect of obesity, a major risk factor for pre-eclampsia, and a condition disproportionately affecting AI/AN women.

Methods—This retrospective cohort study of linked birth-hospital discharge data from Washington State (2003–2013) included all AI/AN women and a sample of White first-time mothers with singleton deliveries. Logistic regression was used to estimate odds ratio (OR) and 95 % confidence intervals (CI) for pre-eclampsia risk in AI/ANs compared to Whites, first controlling for several important risk factors, and subsequently with additional adjustment for pre-pregnancy body mass index (BMI).

Results—AI/ANs had an increased risk of pre-eclampsia compared to Whites after controlling for all covariates except BMI (OR 1.17, 95 % CI 1.06–1.29). After further adjustment for BMI, the racial disparity in pre-eclampsia risk was greatly attenuated (OR 1.05, 95 % CI 0.95–1.16).
Discussion This population-based study suggests that any increased risk in AI/ANs relative to Whites may be at least partly due to differences in BMI.

Keywords

Pre-eclampsia; Body mass index; Overweight; Obesity; American Indian/Alaska Native; Health disparities

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Conflict of Interest

All authors declare that they have no conflict of interest.

Introduction

Hypertensive disorders during pregnancy, such as pre-eclampsia, are the principal cause of maternal morbidity in developed countries (Khan et al. 2006). Pre-eclampsia affects 5–8 % of pregnant women in the US (Boghossian et al. 2014) and has been linked to multiple comorbidities and even mortality in women and fetuses (Rich-Edwards et al. 2014). Known risk factors for pre-eclampsia include obesity, chronic hypertension, gestational diabetes, prior pre-eclampsia, and nulliparity (Pare et al. 2014), whereas prenatal smoking is known to reduce risk (Karumanchi and Levine 2010).

Pre-eclampsia is more prevalent in African Americans than in non-Hispanic Whites (Marshall et al. 2014; Bryant et al. 2010; Ghosh et al. 2014; Caughey et al. 2005), but other racial groups, such as American Indians and Alaska Natives (AI/ANs), have rarely been included in population-based studies of this condition. Although AI/AN women are known to have greater risk of several adverse pregnancy outcomes, including low birth weight, preterm delivery, and maternal mortality (CDC 2001; Denny et al. 2002), a recent review stated that insufficient data were available to determine whether pre-eclampsia was more prevalent in AI/ANs than in other racial and ethnic groups (Bryant et al. 2010). The authors also noted a dearth of information on the presence of racial disparities or the potential role of social, environmental, and behavioral factors in hypertensive disorders during pregnancy in AI/ANs (Bryant et al. 2010). Data from the 2008 Behavioral Risk Factor Surveillance System (BRFSS) indicate that 33 % of AI/AN women of childbearing age are obese, compared to 20 % of Whites (Denny et al. 2002). Additionally, AI/ANs have a higher prevalence of prenatal smoking; lower educational attainment; lower socioeconomic status; and lower rates of prenatal care than their White counterparts (Hwang et al. 2013). Given that AI/AN women of childbearing age exhibit a higher prevalence of several risk factors for pre-eclampsia, relative to Whites (Lisonkova et al. 2013), we hypothesized that AI/ANs would be at increased risk of pre-eclampsia.

Using population-based data for recent deliveries in Washington State, we estimated and compared the prevalence of pre-eclampsia among AI/AN and White first time mothers. Since a recent study concluded that being overweight or obese is “the most important risk factor for pre-eclampsia” (Pare et al. 2014), we assessed the additional effect of adjustment for body mass index (BMI) in this relationship after adjusting for other known risk factors.

Methods

We conducted a retrospective cohort study using data from Washington State linked birth-hospital discharge records for singleton live births to first-time mothers during 2003–2013. State birth records provide data of the demographic characteristics of mothers and infants; the linked hospital discharge records include International Classification of Diseases (ICD-9) diagnosis codes for mothers with birth hospitalizations. Maternal information from the birth certificate was used to assess characteristics including age, parity, singleton/multiple gestation, and prenatal smoking. The presence of pre-eclampsia was determined based on birth certificate checkboxes indicating the presence of pre-eclampsia and/or ICD-9 codes for pre-eclampsia/eclampsia (642.4–642.6). The combination of these sources has

been shown to more accurately identify pregnancy complications (Lydon-Rochelle et al. 2005a, b). Because we used de-identified data, our study was deemed exempt from review by the Washington State Institutional Review Board.

This analysis included all singleton live births to AI/AN women and a randomly selected 10:1 comparison group of all other women with deliveries, frequency matched by delivery year. Race/ethnicity was self-reported by a checkbox in the birth record; 7189 women were identified as AI/AN; 63,886 as White. Because prior studies have variously ignored Hispanic ethnicity status or excluded persons of Hispanic ethnicity, we calculated risk estimates using both approaches; our initial analyses included all AI/ANs and Whites, independent of their Hispanic ethnicity status. Subsequently, we repeated the analysis excluding Hispanics from both groups, to compare non-Hispanic AI/ANs (N = 6088) to non-Hispanic Whites (N = 57,905). We limited our sample to women with singleton pregnancies without prior live births, because multiple gestation and nulliparity are known risk factors for pre-eclampsia (Mostello et al. 2002; Young and Wylie 2012).

Pre-eclampsia/eclampsia was coded dichotomously (yes/no). We examined the following variables from the birth certificate for their possible effects on the relationship of interest: maternal age (12–19, 20–24, 25–29, 30–34, 35–55 years); maternal education (less than high school; high school graduate or GED; and some college or college graduate); BMI, calculated according to WHO standards (underweight = BMI < 18.5; normal 18.5–24.9; overweight 25–29.9; and obese 30+); prenatal smoking (yes/no); marital status (married/single); Medicaid insurance (yes/no); and participation in the Women, Infants, and Children (WIC) program (yes/no).

Analyses were conducted with STATA 13 (StataCorp 2013). Temporal trends in pre-eclampsia occurrence by race were examined as proportions of affected deliveries to all AI/ANs and the sample of White women in each calendar year 2003–2013. Logistic regression was used to calculate odds ratio (OR) estimates of the relative risks of pre-eclampsia risk in AI/ANs compared to Whites, adjusting for the covariates indicated above. We initially calculated ORs with adjustment for all covariates except BMI. We adopted this approach because the AI/AN and White populations have very different demographic and socioeconomic characteristics and distinct prenatal smoking patterns (Hwang et al. 2013; Amparo et al. 2011; Baldwin et al. 2009). A subsequent model adjusted for BMI, because average BMI is higher in AI/ANs than in Whites (CDC 2012), and allowed us to examine its unique effect on pre-eclampsia risk.

Results

Relative to Whites, AI/ANs were generally younger, had lower educational attainment, were more likely to smoke during pregnancy, have Medicaid insurance, and participate in WIC (Table 1). Greater proportions of AI/ANs were also overweight (27 vs 24 %) or obese (28 vs 19 %) than Whites; only 43 % of AI/ANs had normal BMI, compared to 53 % of Whites. Similar proportions (99 % AI/AN; 98 % White) of deliveries occurred in-hospital (data not shown). During the study period, the annual proportions of first-time AI/AN mothers with singleton deliveries complicated by pre-eclampsia were usually slightly greater than those

observed in Whites, but there was no consistent temporal trend (Fig. 1). Over a 10-year period, the prevalence of pre-eclampsia fluctuated between 7 and 11 % in AI/ANs, while it declined slightly from 8 to 7 % in Whites.

AI/ANs had a greater risk of pre-eclampsia than Whites, even after controlling for maternal age, educational attainment, prenatal smoking, marital status, Medicaid insurance, and WIC participation (OR 1.17; 95 % CI 1.06, 1.29) (Table 2). After additional adjustment for BMI, however, the relative risk of pre-eclampsia was attenuated (OR 1.05, 95 % CI 0.95–1.16) and no longer statistically significant. Results did not change after excluding records of Hispanic women in either group from analyses (OR 1.04, 95 % CI 0.93, 1.15, data not shown). AI/ANs who were underweight (OR 1.39, 95 % CI 0.64, 3.02), normal weight (OR 1.02, 95 % CI 0.83, 1.22), overweight (OR 1.23, 95 % CI 0.93, 1.36), or obese (OR 1.00, 95 % CI 0.86, 1.17) generally had relative risks of pre-eclampsia comparable, or slightly (but not statistically significantly) greater than those of their White counterparts (Table 2).

Discussion

AI/AN mothers in Washington State with singleton deliveries during 2003–2013 had a 17 % increased risk of pre-eclampsia, relative to Whites, after adjustment for maternal age, markers of socio-economic status, and prenatal smoking. However, no significantly increased risk was observed after adjustment for BMI, suggesting that the increased risk observed initially was possibly due to confounding by disparate BMI levels in these two groups.

Our results emphasize the importance of BMI in pre-eclampsia risk for both AI/AN and White women. Our findings on AI/ANs expand the limited body of work on pre-eclampsia in AI/ANs that has largely focused on genetic factors (Best et al. 2009, 2012a, b, 2013). Our results are generally consistent with two prior studies of African American, Asian, Caucasian, Hispanic, and Multiracial women on the significance of BMI in pre-eclampsia (Boghossian et al. 2014; Pare et al. 2014). There is, however, evidence that pre-eclampsia risk remains increased in African Americans (Marshall et al. 2014; Bryant et al. 2010), even after controlling for BMI (Ghosh et al. 2014).

Further research is needed to understand the cumulative effect of pre-eclampsia on subsequent pregnancies in AI/ANs. Previous studies have found that prior pre-eclampsia is a risk factor for recurrence (Boghossian et al. 2014; Giannubilo et al. 2014), but AI/ANs were not represented in the study samples. Possible interaction effects between BMI and other health variables also remain unclear. We do not fully understand how unhealthy behaviors, such as sedentary lifestyles or poor diet, can alter the effect of BMI on pre-eclampsia risk. Studies which include sufficient numbers of AI/ANs and with additional information on these aspects may be informative.

This study has several limitations. First, some records lacked BMI data, thereby reducing our original sample. However, the percentage of missing data for BMI did not vary by racial group (9 % AI/AN, 8 % White). The characteristics of AI/AN and White women with, and without missing data for BMI did not demonstrate large differences in maternal age, prenatal

smoking, or Medicaid status. These results suggest that our fully adjusted risk estimate was not biased by differences in women with, and without this information. Second, our analysis treated AI/ANs and Whites as homogeneous groups, without identifying people of mixed race or recognizing the cultural heterogeneity of each population. This approach might have blurred differences in pre-eclampsia risk between tribal communities. Knowledge of any such differences could potentially inform future interventions; it is important to examine disparities in health outcomes across tribal communities as well as racial and ethnic groups to assist in identifying priorities for interventions intended to prevent pre-eclampsia, and other adverse outcomes. Moreover, most participants self-reported their race, but if left blank, medical staff could have filled in racial information, and potentially misclassified mothers and infants.

Third, although the combination of hospital discharge and birth certificate data improved our ability to identify pre-eclampsia compared to birth records only, use of ICD-9 codes to identify pre-eclampsia is still imperfect. Although predictive values and specificity of discharge data for identifying pre-eclampsia are often assessed at 70 % or greater (Lydon-Rochelle et al. 2005a; Klemmensen et al. 2007; Yasmeen et al. 2006) and as high as 98.5 % when identified during a hospitalization (Palmsten et al. 2014), some studies report levels as low as 54 % and have demonstrated charting and diagnostic errors in their use (Geller et al. 2004). However, we have no reason to believe that misclassification occurred differentially by race. With respect to the other variables, maternal age and parity in birth records has been assessed as accurate (Roohan et al. 2003). Although prenatal smoking is typically under-reported (Allen et al. 2008), the direction of any biases due to misclassification of smoking as a confounder in our results is unclear, if it is differentially reported by race. Clinically measured BMI from the prenatal care record, typically the source of information for the birth certificate, is probably accurate. However, if weight had been self-reported in some instances, it might contain inaccuracies due to under-reporting (Lin et al. 2012). Unfortunately, we had no information about the extent to which weight was self-reported.

Finally, we had no data about the severity of pre-eclampsia or the potential contribution of family history. Previous studies have shown that severe pre-eclampsia has devastating implications for women and infants, and that BMI could be a contributing factor (Heida et al. 2012). Additionally, a parallel line of inquiry showed that having a mother or sister with pre-eclampsia doubled pre-eclampsia risk (Lie et al. 1998). Our omission of covariates for the severity of pre-eclampsia or family history might have led to an over-representation of the effect of BMI in our analyses. Studies with information on severity of pre-eclampsia and family history will be important.

Despite these limitations, our study has important strengths. No previous population-based research has estimated the relative risk of pre-eclampsia in AI/ANs and Whites, or the relative effect of demographic and socioeconomic covariates, prenatal smoking, and BMI. We identified a large and recent population sample to examine the association between BMI and pre-eclampsia risk in AI/ANs. Finally, unlike studies reliant on self-reported information exclusively, our data were uniformly collected around the time of delivery, much of it from medical records, and none of it reliant on recall.

Pre-eclampsia is a major cause of maternal morbidity in the US, and obesity is an important risk factor for this condition in AI/AN, White, and likely other groups. It is important to develop culturally-specific and appropriate interventions in order to decrease the risk of this serious condition in AI/AN women. Community-based participatory research is expected to help identify points of intervention to prevent pre-eclampsia risk in this population. Meanwhile, our results provide a rationale for researchers in endocrinology, gynecology, obstetrics, and AI/AN health to collaborate on lowering pre-eclampsia risk by reducing the prevalence of obesity in women of reproductive age across all races.

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Significance

What is already known on this subject?

The prevalence of pre-eclampsia varies by race, and no study to date has examined this condition in American Indians/Alaska Natives (AI/ANs). Obesity is a known risk factor for pre-eclampsia and AI/AN women have a higher prevalence of obesity than women of other races.

What this study adds?

The modestly increased pre-eclampsia risk observed for AI/AN women was greatly attenuated after adjusting for BMI. Efforts to prevent obesity among women of childbearing age may reduce pre-eclampsia risk in AI/AN and White women.

Fig. 1. Percentage of first-time American Indian/Alaska Native and White mothers with singleton live births diagnosed with pre-eclampsia in Washington State (2003–2013)

Table 1

Selected characteristics of American Indian/Alaska Native and White first-time mothers with singleton live births in Washington State, 2003–2013

Characteristic	AI/AN (N = 7194)		White (N = 63,886)	
	n ^a	%	n ^a	%
Age (years)				
12–19	2670	37.1	8638	13.5
20–24	2713	37.7	18,708	29.3
25–29	1101	15.3	17,853	28.0
30–34	488	6.8	12,522	19.6
35–55	221	3.1	6152	9.6
Educational attainment				
<High school	2543	35.7	7804	12.3
High school graduate or GED	2280	32.0	14,317	22.5
Some college or college graduate	2309	32.4	41,411	65.2
BMI				
<18.5	177	2.7	2057	3.5
18.5–24.9	2694	41.4	30,595	52.1
25.0–29.9	1799	27.6	14,379	24.5
30	1839	28.3	11,708	19.9
Prenatal smoking				
No	5729	80.3	56,484	89.2
Yes	1409	19.7	6862	10.8
Marital status				
Married	1680	23.4	40,815	64.0
Single	5490	76.6	22,982	36.0
Medicaid health insurance				
No	2508	35.6	43,610	70.0
Yes	4542	64.4	18,722	30.0
WIC participation				
No	2133	32.6	38,573	66.4
Yes	4412	67.4	19,516	33.6

^aNumbers may not add to totals because of missing data

Table 2

Preeclampsia among American Indian/Alaska Native and White first-time mothers with singleton live births, overall and by maternal body mass index category, Washington State, 2003–2013

	N	<u>Preeclampsia</u> n	<u>OR^a</u> (%)	(95 % CI)	<u>OR^b</u>	(95 % CI)
All women						
White	62,987	4985	(7.9)	1.00	(Ref)	1.00 (Ref)
AI/AN	7109	619	(8.7)	1.17	(1.06–1.29)	1.05 (0.95–1.16)
By BMI						
<18.5						
White	2034	76	(3.7)	1.00	(ref)	
AI/AN	176	8	(4.6)	1.39	(0.64–3.02)	
18.5–<24.9						
White	30,251	1609	(5.3)	1.00	(Ref)	
AI/AN	2673	151	(5.6)	1.02	(0.83–1.22)	
25–<29.9						
White	14,213	1266	(8.9)	1.00	(Ref)	
AI/AN	1778	163	(9.2)	1.23	(0.93–1.36)	
30						
White	11,582	1709	(14.8)	1.00	(Ref)	
AI/AN	1823	250	(13.7)	1.00	(0.86–1.17)	

^a Adjusted for birth year, maternal age, educational attainment, marital status, Medicaid insurance, WIC participation, and prenatal smoking

^b Adjusted for birth year, maternal age, educational attainment, marital status, Medicaid insurance, WIC participation, prenatal smoking, and BMI