Differential Risk of Hypertensive Disorders of Pregnancy among Hispanic Women

MYLES WOLF,* ANAND SHAH,‡ RICARDO JIMENEZ-KIMBLE,* JENNY SAUK,* JEFFREY L. ECKER,† and RAVI THADHANI*†

Departments of *Medicine and †Obstetrics and Gynecology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; and ‡Centre for International Health, Faculty of Medicine, University of Toronto, Ontario, Canada.

Abstract. Preeclampsia and gestational hypertension are leading complications of pregnancy that also portend increased risk of future chronic hypertension. Although rates of chronic hypertension differ between non-Hispanic Caucasian and Hispanic women, few studies have examined their relative rates of hypertensive disorders of pregnancy. The purpose of this study was to compare the risk of preeclampsia and gestational hypertension in a prospective cohort of normotensive, nulliparous Hispanic (n = 863) and non-Hispanic Caucasian women (n = 2,381). Compared with non-Hispanic Caucasian women, Hispanic women demonstrated a significantly decreased incidence of gestational hypertension (1.6% versus 8.5%; P < 0.01), but a similar incidence of preeclampsia (3.8% versus 3.7%; P = 0.9). Adjusting for age, smoking, diabetes, BP, body mass index (BMI), and multiple gestation uncovered an increased relative risk (RR) for preeclampsia among Hispanic women (RR 1.9; 95% CI, 1.1 to 3.3; P = 0.01), while their relative risk for gestational hypertension remained significantly decreased (RR 0.39; 95% CI, 0.22 to 0.72; P < 0.01). Among women who initially presented with hypertension during pregnancy, Hispanic women were over threefold (hazard ratio 3.3; 95% CI, 1.9 to 6.0; P < 0.01) more likely to develop preeclampsia than non-Hispanic Caucasian women. Besides Hispanic ethnicity, baseline BP, BMI, diabetes, and multiple gestation were independent risk factors for preeclampsia, whereas only baseline BP and BMI were associated with gestational hypertension. Socioeconomic status and access to prenatal care were not associated with either disorder. Hispanic ethnicity is independently associated with increased risk for preeclampsia and decreased risk for gestational hypertension. The initial presentation of hypertension during pregnancy in Hispanic women most likely represents early preeclampsia.

The hypertensive disorders of pregnancy, preeclampsia, and gestational hypertension, which complicate 6 to 8% of pregnancies (1), are leading causes of maternal and fetal morbidity and mortality, and are associated with increased risk of future chronic hypertension (2). Although the characteristic placental pathology of preeclampsia is established during early pregnancy (3), there are no reliable tools for early clinical diagnosis and no effective therapies to prevent disease or improve maternal and fetal outcomes. Importantly, there are also no means to differentiate whether the new onset of hypertension during pregnancy represents gestational hypertension or preeclampsia in which proteinuria has yet to develop. More fundamentally, it remains unclear if preeclampsia and gestational hypertension represent ends of a single pathophysiologic spectrum of pregnancy-induced hypertension or distinct disorders with unique biological pathways and differential risk factor profiles.

Risk factors for preeclampsia have been studied extensively as preeclampsia is the hypertensive disorder of pregnancy most commonly associated with devastating complications. Nulliparity, obesity, insulin resistance, multiple gestation, preexisting hypertension or diabetes mellitus, and gestational diabetes mellitus (GDM) are consistently identified as risk factors for preeclampsia (4–20). The risk associated with race-ethnicity is less clear. Hispanic women demonstrate increased rates of obesity, insulin resistance, type 2 diabetes mellitus, and GDM compared with non-Hispanic Caucasian women (21,22), suggesting that they might be at increased risk of preeclampsia. Few studies, however, examined the risk among Hispanic women in those that did, Hispanic and African-American women were often grouped together precluding detailed conclusions (15).

In contrast to preeclampsia, gestational hypertension is often considered a benign condition. However, gestational hypertension is associated with adverse outcomes such as increased Cesarean section rates and decreased birth weight (23–25); like preeclampsia, gestational hypertension also portends increased risk of future chronic hypertension (2). Nonetheless, only a small fraction of studies of hypertensive disorders of pregnancy focused specifically on gestational hypertension. Consequently, far less is known about risk factors for gestational hypertension, how these differ from risk factors for preeclampsia, and whether race-ethnicity is a risk factor for either disorder. In prior case-control studies, we observed a reduced risk of...
gestational hypertension among Hispanic women compared with non-Hispanic Caucasian women (26), but the risk of preeclampsia was similar between the two groups (20). The purposes of this study were therefore to compare the incidence and relative risks (RR) of preeclampsia and gestational hypertension among Hispanic and non-Hispanic Caucasian women, to examine risk factors for each disorder, and to address the impact of socioeconomic status and access to prenatal care on the development of hypertensive disorders of pregnancy.

Materials and Methods

Study Population
The Massachusetts General Hospital Obstetric Maternal Study (MOMS) is a prospective cohort study of risk factors for hypertensive disorders of pregnancy and GDM. All women who receive prenatal care through the Massachusetts General Hospital (MGH) obstetrics service are included in the cohort. The MGH obstetrics service provides primary prenatal care to an ethnically and socioeconomically diverse population at its main campus in Boston and at several affiliated health centers in surrounding neighborhoods. Overall, 21% of patients who receive care at the MGH and its affiliated centers live below the poverty line. All prenatal care and delivery data is collected prospectively at the point of care by health providers and entered into an electronic medical record that serves as the primary medical record during pregnancy. The electronic medical record (EMR) contains details regarding patient demographics, past medical and obstetric history, prenatal visit data, all BP measurements and urinalysis results, laboratory data, and pregnancy outcome data. Data from the EMR is downloaded directly to a research-grade database used for MOMS. Race-ethnicity is ascertained by patient self-report and categorized as non-Hispanic Caucasian, Hispanic, African-American, Asian, or Other. The Hispanic population served by MGH is mostly Caucasian and originates primarily from Central or South America (65%), Puerto Rico (28%), and Mexico (7%).

All nulliparous, normotensive, non-proteinuric Hispanic (n = 863) and non-Hispanic Caucasian women (n = 2381) who received prenatal care and delivered at MGH between October 1998 and January 2002 were included in the current study. Women with preexisting proteinuria or chronic hypertension, defined as BP ≥ 140/90 mmHg or antihypertensive therapy that preceded pregnancy or first appeared before 20 wk of gestation (1) were excluded.

Primary Exposure and Outcomes
The primary exposure was ethnicity, either Hispanic or non-Hispanic Caucasian. The primary outcomes were preeclampsia and gestational hypertension defined according to research criteria (1) using BP recordings from prenatal visits; measurements during labor were not used to define pregnancy outcomes. Preeclampsia was defined as the new onset of hypertension (BP ≥ 140/90 mmHg) after 20 wk of gestation in association with proteinuria, either ≥ 2+ by dipstick or ≥ 300 mg/24 h in the absence of urinary infection. Gestational hypertension was defined as the new onset of isolated hypertension that first appeared after 20 wk of gestation (1). Blood pressures were measured from subjects’ right arm using standard sphygmomanometers after they were seated at rest for 3 to 5 min. After selecting the proper cuff size on the basis of right midarm circumference, BP readings that coincided with the timing of the first (systolic) and fifth (diastolic) Korotkoff sounds were recorded. Hypertensive BP readings were repeated 5 to 10 minutes later; if the subsequent readings were also elevated, they were recorded in the EMR.

Covariates
To investigate potential confounding, we examined women’s age, baseline BP, and body mass index (BMI: weight in kg/height in m^2) at the time of their first prenatal visit, their self-reported smoking status (never, prior or current), number of fetuses (singleton or multiple), and diabetes status (preexisting/ gestational or neither). Excluding women with preexisting diabetes mellitus, 96% of women underwent third trimester gestational diabetes mellitus (GDM) screening using 50-g oral glucose-loading tests followed by diagnostic, 3-h, 100-g glucose tolerance tests (GTT) (27). Gestational diabetes was diagnosed when two or more of the four hourly GTT glucose levels exceeded the following thresholds: fasting ≥ 105 (5.8), 1-h ≥ 190 (10.5), 2-h ≥ 165 (9.1), 3-h ≥ 145 mg/dL (8.0 mmol/L) (27). To assess potential confounding by socioeconomic status, we examined marital status (single or married), insurance (private or Medicaid/none), years of education and income. Income was ascertained by cross-referencing individual women’s ZIP code with the corresponding ZIP code’s median household income defined by the 2000 United States Census (28) as has been done in prior studies (13). Access to prenatal care was inferred from the gestational age and trimester of the first prenatal visit as has been done in prior studies (29) and from tabulating each woman’s total number of routinely scheduled prenatal visits with her obstetrician or midwife.

Statistical Analyses
Two-sample t tests or χ^2 tests were used to compare baseline and delivery characteristics, indicators of socioeconomic status, access to prenatal care, and the crude incidence of hypertensive disorders of pregnancy among Hispanic and non-Hispanic Caucasian women. Logistic regression and stratified analyses were used to calculate the RR of hypertensive disorders of pregnancy while adjusting for potential confounding and investigate the effects of socioeconomic status and access to prenatal care. All multivariable analyses were adjusted for gestational age at the time of the first prenatal visit in order to account for variation in baseline BP and BMI that was associated with differences in the gestational age when they were measured. Multiple linear regression was used to examine independent predictors of fetal birth weight.

In women with preeclampsia, hypertension may develop before proteinuria. Therefore, in certain cases of incipient preeclampsia, delivery may occur before the detection of proteinuria; thus, preeclampsia may be misclassified as gestational hypertension. To investigate the potential for this form of misclassification bias, we examined the relative timing of the appearance of hypertension and proteinuria and reanalyzed the data after excluding women who presented with hypertension near term and were thus most at risk to be misclassified. We compared the Kaplan-Meier estimates and hazard ratio (HR) of the likelihood of Hispanic and non-Hispanic women remaining free from developing preeclampsia after hypertension first manifested. In these time-to-event analyses, time = 0 was when hypertension first presented, and women who did not develop proteinuria were censored at the time of delivery. All analyses were performed using Intercooled Stata 7.0 (Stata Corporation, College Station, TX). Two-sided P values < 0.05 were considered statistically significant.

Results

Baseline and Delivery Characteristics, Socioeconomic Status, and Access to Prenatal Care
Baseline and delivery characteristics and indicators of socioeconomic status and access to prenatal care comparing the Hispanic and non-Hispanic Caucasian groups are presented in
Table 1. Hispanic women were younger, heavier, and more likely to be current smokers. Despite their higher BMI, they displayed significantly lower baseline BP. Fertility treatment and multiple gestation were more common among non-Hispanic Caucasian women. Hispanic women demonstrated significantly lower mean income and education levels and were significantly less likely to be married or privately insured. Although Hispanic women were more likely to present later for their initial prenatal care visit, there were no differences in their total number of routinely scheduled prenatal visits. While there were no differences between the groups' gestational age at delivery, incidence of preterm delivery, or fetal death rates, Hispanic women delivered lower–birth weight babies and were less likely to deliver by Cesarean section.

Table 1. Pregnancy characteristics of Hispanic and non-Hispanic Caucasian women

<table>
<thead>
<tr>
<th></th>
<th>Hispanic</th>
<th>Caucasian</th>
<th>P*</th>
</tr>
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<tbody>
<tr>
<td><strong>Baseline characteristics at the first prenatal visit</strong></td>
<td></td>
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</tr>
<tr>
<td>age (yr)</td>
<td>22.6 ± 5.2</td>
<td>30.0 ± 5.4</td>
<td>&lt;0.01</td>
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<tr>
<td>body mass index (kg/m²)</td>
<td>25.6 ± 5.4</td>
<td>24.5 ± 4.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>smoking (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>never</td>
<td>44</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>stopped</td>
<td>10</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>current</td>
<td>46</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>systolic BP (mmHg)</td>
<td>107 ± 11</td>
<td>113 ± 11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>diastolic BP (mmHg)</td>
<td>65 ± 8</td>
<td>71 ± 8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>mean arterial BP (mmHg)b</td>
<td>79 ± 8</td>
<td>85 ± 8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>number of fetuses (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>singleton</td>
<td>99</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>multiple</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>fertility treatment (%)</td>
<td>0.4</td>
<td>7.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
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<td></td>
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<tr>
<td>preexisting diabetes (%)</td>
<td>0</td>
<td>0.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>gestational diabetes (%)</td>
<td>2.6</td>
<td>2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Maternal socioeconomic status</td>
<td></td>
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<td></td>
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<tr>
<td>income ($)</td>
<td>34,548 ± 9579</td>
<td>58,604 ± 20,879</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>education (yr)</td>
<td>11 ± 4</td>
<td>16 ± 3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>insurance (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>private</td>
<td>24</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Medicaid/none</td>
<td>76</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>marital status (%)</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
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<tr>
<td>married</td>
<td>30</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>single</td>
<td>70</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Access to prenatal care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gestational age at first prenatal visit (wk)</td>
<td>11.7 (9.1 to 17.4)</td>
<td>11.0 (9.7 to 12.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>trimester of first prenatal visit (%)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1st trimester</td>
<td>70</td>
<td>89</td>
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</tr>
<tr>
<td>2nd trimester</td>
<td>22</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>3rd trimester</td>
<td>8</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>visits (#)</td>
<td>12 ± 3</td>
<td>12 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>Delivery characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gestational age (wk)</td>
<td>39.7 (38.7 to 40.7)</td>
<td>39.7 (38.7 to 40.7)</td>
<td>NS</td>
</tr>
<tr>
<td>preterm delivery (% &lt;38 wk)</td>
<td>13</td>
<td>16</td>
<td>NS</td>
</tr>
<tr>
<td>fetal death (%)</td>
<td>0.6</td>
<td>0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Cesarean section (%)</td>
<td>16</td>
<td>26</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>birth weight (g)</td>
<td>3231 ± 525</td>
<td>3373 ± 578</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Continuous variables are reported as mean ± SD or median (interquartile range) as appropriate.

* NS, not statistically significant.

b Mean arterial BP = (systolic BP + 2(diastolic BP))/3.

f Visits refer to the number of routinely scheduled visits with obstetricians or midwives and excludes emergency, urgent care, or unscheduled walk-in visits.
Crude Incidence of Hypertensive Disorders of Pregnancy

The crude incidence of preeclampsia and gestational hypertension according to ethnicity are displayed in Figure 1. Compared with non-Hispanic Caucasian women, Hispanic women displayed significantly decreased rates of gestational hypertension (1.6% versus 8.5%; \( P < 0.01 \)) but similar rates of preeclampsia (3.8% versus 3.7%; \( P = 0.9 \)). At the time when hypertension first manifested, the mean BP for Hispanic women ultimately diagnosed with preeclampsia and gestational hypertension were 151 ± 7/97 ± 5 and 150 ± 1/97 ± 8, respectively; similarly, for Caucasian women, they were 150 ± 7/97 ± 7 and 146 ± 8/95 ± 6, respectively. Therefore, the degree of hypertension at the time of diagnosis did not discriminate early preeclampsia from gestational hypertension.

Multivariable Analysis of Risk Factors for Preeclampsia and Gestational Hypertension

After adjusting for age, baseline BP and BMI, smoking, gestational age at the first prenatal visit, multiple gestation, and preexisting diabetes mellitus or GDM, Hispanic women’s RR of preeclampsia increased from 1.0 (95% CI, 0.7 to 1.6; \( P = 0.9 \)) to 1.9 (95% CI, 1.1 to 3.3; \( P = 0.01 \)), indicating the presence of substantial negative confounding. Baseline BP was the primary negative confounder along with age and multiple gestation; removing these variables from the model reduced the RR towards the unadjusted estimate. In the adjusted model, BP (RR 1.6 per 5 mmHg mean arterial pressure; 95% CI, 1.4 to 1.8; \( P < 0.01 \)), BMI (RR 1.07 per kg/m²; 95% CI, 1.04 to 1.10; \( P < 0.01 \)), multiple gestation (RR 2.3 compared with singleton; 95% CI, 1.0 to 5.4; \( P = 0.04 \)), and preexisting diabetes or GDM (RR 2.5 compared with euglycemic women; 95% CI, 1.2 to 5.0; \( P = 0.01 \)) were also independently associated with preeclampsia.

Hispanic women’s unadjusted RR of developing gestational hypertension compared with Caucasian women was 0.18 (95% CI, 0.10 to 0.30; \( P < 0.01 \)), and this remained statistically significant (RR 0.39; 95% CI, 0.22 to 0.72; \( P < 0.01 \)) after adjusting for the same group of potential confounders. Unlike preeclampsia, baseline BP (RR 1.7 per 5 mmHg mean arterial pressure; 95% CI, 1.5 to 1.9; \( P < 0.01 \)) and BMI (RR 1.04 per kg/m²; 95% CI, 1.01 to 1.07; \( P < 0.01 \)) were the only other independent risk factors for gestational hypertension. Excluding women with identifiable medical conditions associated with hypertensive disorders of pregnancy, such as diabetes mellitus, GDM, multiple gestation and placental abnormalities (38 of the 338 total hypertensive women), did not appreciably alter the results (data not shown).

In the multivariable models, there was no independent association between age and either preeclampsia (RR 1.03 per 5-yr increase; \( P = 0.8 \)) or gestational hypertension (RR 1.11 per 5-yr increase; \( P = 0.2 \)). Nonetheless, Hispanic women were significantly younger than non-Hispanic Caucasian women; therefore, we performed stratified analyses of younger (age < 25 yr) and older (age ≥ 25 yr) mothers to test for residual confounding by maternal age. The point estimates of Hispanic women’s RR for preeclampsia were 2.6 and 1.9 in younger and older mothers, respectively; for gestational hypertension they were 0.20 and 0.47, respectively. These estimates were qualitatively similar to the overall model’s estimates, suggesting that differences in maternal age did not confound the primary analyses. Interestingly, although crude rates of GDM did not differ between Hispanic and non-Hispanic Caucasian women (2.6% versus 2.5%; \( P = NS \)), Hispanic women’s multivariable-adjusted RR of GDM increased to 2.6 (95% CI, 1.4 to 4.9; \( P < 0.01 \)), primarily following adjustment for maternal age.

Timing of Hypertension and Proteinuria

The median gestational age when hypertension first developed was 35.8 and 36.4 wk for preeclampsia and gestational hypertension, respectively. The median gestational age when proteinuria first appeared in women with preeclampsia was 36.1 wk. Among women with gestational hypertension, the median gestational age at delivery was 39.4 wk; the median window of time between their development of hypertension and delivery was 2.8 wk. Using this window as a reference, 82% of women with preeclampsia developed both hypertension and proteinuria within 2.8 wk of one another, whereas proteinuria preceded hypertension by more than 2.8 wk in only 3%. Hypertension preceded proteinuria by more than 2.8 wk in the remaining 15%. Therefore, women with gestational hypertension remained pregnant for a timeframe during which 85% of women with preeclampsia had already manifested both proteinuria and hypertension, suggesting that most women ultimately diagnosed with gestational hypertension had sufficient temporal “opportunity” to develop proteinuria and hence, preeclampsia.

On the basis of these observations, we reexamined the multivariable-adjusted models for preeclampsia and gestational hypertension after excluding women in whom hypertension first appeared after 37 wk of gestation, the difference between the median gestational age of delivery among normotensive women and the median window of time between the
development of hypertension and delivery among women diagnosed with gestational hypertension. This served to exclude hypertensive women who may not have had ample time to develop proteinuria and who were therefore the most likely to be misclassified. In these models, the RR comparing Hispanic women with non-Hispanic Caucasian women were 2.0 (95% CI, 1.2 to 3.4; P = 0.01) for preeclampsia and 0.11 (95% CI, 0.03 to 0.46; P < 0.01) for gestational hypertension. These estimates were qualitatively similar and indeed more divergent relative to the overall models’ risk estimates. In a Kaplan-Meier analysis of the likelihood of remaining free from preeclampsia after hypertension first manifested (Figure 2), there was an early and progressive separation of the Hispanic and non-Hispanic Caucasian curves (P < 0.01). The HR for developing preeclampsia comparing Hispanic women with non-Hispanic Caucasian women was 3.3 (95% CI, 1.9 to 6.0; P < 0.01), and excluding the women with late onset hypertension (> 37 wk) further magnified Hispanic women’s HR to 4.4 (95% CI, 2.4 to 7.8; P < 0.01), indicating that the initial presentation of hypertension during pregnancy in Hispanic women was significantly more likely to represent preeclampsia compared with a similar presentation in non-Hispanic Caucasian women.

Effects of Socioeconomic Status and Access to Prenatal Care

To investigate whether differences in socioeconomic status or access to prenatal care accounted for the differences in rates of hypertensive disorders of pregnancy, we stratified women by ethnicity and compared indicators of socioeconomic status and access to prenatal care among women who developed hypertensive disorders of pregnancy and those who remained normotensive (Table 2). Within both ethnicity strata, there were minimal differences in income, education, marital status, timing of the first prenatal visit and total number of prenatal visits comparing the hypertensive and normotensive groups. Within both ethnicity strata, women who developed hypertension were more likely to be privately insured, raising the possibility that more vigilant diagnosis of hypertensive disorders of pregnancy among privately insured women could have biased the primary results. However, there were no differences in the mean number of prenatal visits between Medicaid/uninsured and privately insured women (12.0 ± 3.4 versus 12.1 ± 2.7 visits), and the BP and urinalysis results used to classify pregnancy outcome were measured in all women at all visits. Furthermore, the point estimates for risk of preeclampsia and gestational hypertension among Hispanic women were qualitatively unchanged when Medicaid/uninsured and privately insured women were examined separately in stratified models (data not shown). Thus, although there were large differences in socioeconomic status between the unstratified ethnic groups (Table 1), there was no evidence within each group that low socioeconomic status or insufficient access to prenatal care affected risk of disease.

Birth Weight

In univariate analyses, women with preeclampsia delivered significantly lower birth weight babies at earlier median gestational ages (2964 ± 738 g at 38.0 wk; P < 0.01) compared with normotensive women (3344 ± 559 g at 39.7 wk) and women with gestational hypertension (3410 ± 498 g at 39.4 wk). Hispanic babies were 142 g smaller than non-Hispanic Caucasian babies irrespective of pregnancy outcome (Table 1). In a multiple linear regression model, factors that were independently associated with birth weight included (in descending order of statistical significance) gestational age of delivery (179-g increase per wk; P < 0.01), maternal height (23-g increase per inch; < 0.01), diabetes-GDM (308-g increase compared with euglycemic women; P < 0.01), and smoking (40-g decrease compared with nonsmokers; P = 0.03). In the model, there remained only a trend toward smaller babies among women with preeclampsia (75-g decrease compared with normotensive; P = 0.09), mostly due to adjusting for gestational age of delivery. Likewise, the decreased birth weight among Hispanic women was attenuated (35-g decrease compared with Caucasians; P = 0.10), mostly due to adjusting for maternal height. There was no difference in adjusted birth weight between women with gestational hypertension and normotensive women.

Discussion

In this prospective study of over 3200 women, we identified significantly increased risk of preeclampsia and decreased risk of gestational hypertension among Hispanic women relative to non-Hispanic Caucasians. Whereas several epidemiological studies have examined the association between race-ethnicity and preeclampsia, this is among the first to examine Hispanic women in detail. Furthermore, few prior prospective studies have simultaneously examined risk factors for gestational hypertension and preeclampsia. While these results should be validated in other pregnancy cohorts, they highlight Hispanic
women’s differential susceptibility to specific hypertensive disorders of pregnancy and, on the basis of the differential risk factor profiles, suggest that despite the obvious similarity between gestational hypertension and preeclampsia, important differences likely exist in the pathogenesis of the two disorders.

Although several risk factors for hypertensive disorders of pregnancy have been firmly established, the risk attributable to specific race-ethnicities is less clear. For example, some studies suggest that African American women are at increased risk of preeclampsia relative to Caucasian women (10–14), but other studies found no difference (17–19). Studies in Australia suggested a reduced risk of preeclampsia among Vietnamese immigrants compared with native Caucasian women (30–32), while others revealed higher preeclampsia rates among the Pacific Islanders (33). Much of these discrepancies may relate to study methodology. Prior studies were small or retrospective (10,15,34), and others relied on ICD-9 codes (17,18) or patient self-report for classification of pregnancy outcome (13), techniques that are prone to misclassification and recall bias (35).

In others, preeclampsia and gestational hypertension were not consistently defined or differentiated, and women with chronic hypertension were often included in the analyses. Prior studies of Hispanic women are similarly sparse and inconsistent, in part, because Hispanic and African-American women were grouped together in certain studies (15) while others did not adjust for potential confounding (13).

While one might suspect that socioeconomic status and access to prenatal care would account for differences in individual race-ethnicity rates of hypertensive disorders of pregnancy, the literature is again controversial (10). Some studies suggest lower levels of education (11,15), single mothers (10,36), decreased access to care (36), and non-private or no medical insurance (13) are associated with increased risk of preeclampsia, but others report no effect of socioeconomic factors (8,14). In this study, we investigated in detail each of these indicators along with median household income. Although there were large differences in socioeconomic status between the two ethnic groups, the stratified analyses suggest that socioeconomic status and access to care exerted minimal effects on the risk of developing hypertensive disorders of pregnancy. We acknowledge, however, that we cannot definitively exclude residual confounding by unmeasured factors associated with access to prenatal care or socioeconomic status, such as psychosocial stressors, nutrition, or exercise.

It could be argued that gestational hypertension simply represents an early stage or mild form of preeclampsia, which with long enough gestation would eventually “progress” to preeclampsia. Even if they are accepted to be distinct conditions, because hypertensive disorders of pregnancy usually present during the latter stages of pregnancy and because other processes may lead to early delivery, certain cases of preeclampsia may be misclassified as gestational hypertension if delivery...
strengthens the observed divergence in Hispanic women’s relative protection from gestational hypertension may be an early manifestation of their decreased propensity for chronic hypertension while their excess preeclampsia may reflect a predisposition to future renal injury. Indeed, hypertension and diabetes during pregnancy are strong predictors of future chronic hypertension and type 2 diabetes mellitus after pregnancy (2,21). It is interesting to speculate whether preeclampsia might likewise identify Hispanic women at increased risk of future ESRD. If so, understanding mechanisms of renal injury during pregnancy might present a unique opportunity to examine novel mechanisms of chronic kidney disease. Perhaps ethnic differences in expression of angiogenic factors, which are mechanistically linked to preeclampsia but not gestational hypertension (3,37) and have been associated with renal injury outside pregnancy (42), might underlie the differential rates of hypertensive disorders of pregnancy we observed.

The strengths of the current study are its prospective design, large sample size, use of research-specific criteria for classification and analysis of both preeclampsia and gestational hypertension, and the exclusion of women with chronic hypertension. In addition, all women received prenatal care contemporaneously within one hospital system thereby limiting region-to-region and time-dependent variability. Nevertheless, this study represents a single center’s experience; therefore, our results should be verified in other populations. Another limitation is that, although we were able to examine Hispanic women in detail, limited sample sizes precluded investigation of African-American and Asian women. Furthermore, the Hispanic population in our cohort was largely of Central and South American origin; generalization to other Hispanic populations, such as Mexican-Americans, may not be valid. Finally, we classified pregnancies according to maternal ethnicity but were unable to account for paternity. While parental factors have been linked to altered preeclampsia risk in some but not all prior studies (43–45), there is minimal data regarding the effects of paternal race-ethnicity.

Lastly, the clinical relevance of these results deserves mention. There are currently no means for obstetricians or consulting nephrologists to predict which cases of new onset hypertension during pregnancy represent preeclampsia and which will remain non-proteinuric and thus be ultimately labeled as gestational hypertension. As a result, women with gestational hypertension are exposed to potentially unnecessary obstetric morbidity, including early delivery and increased Cesarean section rates similar to women with preeclampsia (23,46). The results of this study suggest that new-onset hypertension during pregnancy in Hispanic women most likely represents incipient preeclampsia. This is in agreement with a prior study in which Hispanic women displayed the greatest rate of “progression” from hypertension to preeclampsia compared with other race-ethnicity groups (47). Whether gestational hypertension and preeclampsia truly represent progressive stages of a single disease spectrum or instead, as suggested by this study, pathophysiologically distinct processes linked coincidentally by similar phenotypic expressions of hypertension is an important yet mostly unanswered question with significant implications for women’s health both during and after pregnancy. Further epidemiologic, physiologic, and genetic studies are needed before definitive conclusions about the relationship (or lack thereof) between preeclampsia and gestational hypertension can be drawn.

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