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Racial/ethnic disparities in the association between preeclampsia risk factors and preeclampsia among women residing in Hawaii

Kazuma Nakagawa, MD^{1,2}, Eunjung Lim, PhD³, Scott Harvey, MD, MS^{1,4}, Jill Miyamura, PhD⁵, and Deborah T. Juarez, ScD⁶

¹The Queen's Medical Center, Honolulu, HI

²Department of Medicine, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI

³Office of Biostatistics & Quantitative Health Sciences, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI

⁴Department of Obstetrics and Gynecology, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI

⁵Hawai'i Health Information Corporation, Honolulu, HI

⁶Daniel K. Inouye College of Pharmacy, University of Hawaii, Hilo, HI

Abstract

Objective—To assess differences in the rates of preeclampsia among a multiethnic population in Hawaii.

Methods—We performed a retrospective study on statewide inpatient data for delivery hospitalizations in Hawaii between January 1995 and December 2013. Multivariable logistic regression was used to assess the impact of maternal race/ethnicity on the rates of preeclampsia after adjusting for age, multiple gestation, multiparity, chronic hypertension, pregestational diabetes, obesity and smoking.

Results—A total of 271,569 hospital discharges for delivery were studied. The rates of preeclampsia ranged from 2.0% for Chinese to 4.6% for Filipinos. Preeclampsia rates were higher among Native Hawaiians who are age <35 and non-obese (OR, 1.54; 95% CI, 1.43-1.66), age 35 and non-obese (OR, 2.31; 95% CI, 2.00-2.68), age 35 and obese (OR, 1.80; 95% CI, 1.24-2.60); other Pacific Islanders who are age <35 and non-obese (OR, 1.40; 95% CI, 1.27-1.54), age 35 and non-obese (OR, 2.18; 95% CI, 1.79-2.64), age 35 and obese (OR, 1.68; 95% CI, 1.14-2.49); and Filipinos who are age <35 and non-obese (OR, 1.55; 95% CI, 1.43-1.67), age 35 and non-obese (OR, 2.26; 95% CI, 1.97-2.60), age 35 and obese (OR, 1.64; 95% CI, 1.04-2.59) compared to whites. Pregestational diabetes (OR, 3.41; 95% CI, 3.02-3.85), chronic hypertension (OR, 5.98;

Corresponding Author: Kazuma Nakagawa, MD, The Queen's Medical Center, 1301 Punchbowl Street, Honolulu, HI 96813, Phone: (808) 691-7152 / Fax: (808) 691-4001, kazuma.nakagawa@hawaii.edu.

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95% CI, 4.98-7.18), and smoking (OR, 1.19; 95% CI, 1.07-1.33) were also independently associated with preeclampsia.

Conclusion—In Hawaii, Native Hawaiians, other Pacific Islanders and Filipinos have a higher risk of preeclampsia compared to whites. For these high-risk ethnic groups, more frequent monitoring for preeclampsia may be needed.

Keywords

Preeclampsia; Eclampsia; Health care disparities; Minority health

Introduction

Preeclampsia is a leading cause of maternal and fetal morbidity and mortality (Khan, Wojdyla, Say, Gulmezoglu, & Van Look, 2006; Steegers, von Dadelszen, Duvekot, & Pijnenborg, 2010). Preeclampsia has been suggested to be a pregnant woman's hypertensive disorder in response to abnormal placentation, inadequate trophoblastic invasion of the spiral arteries, placental atherosclerosis, and placental paracrine effect (Lain & Roberts, 2002). Although the exact etiology of preeclampsia remains unclear, several risk factors have been identified including nulliparity, maternal age, multiple gestation, obesity, pregestational diabetes, pre-existing hypertension and prior history of preeclampsia (Bodnar, Ness, Markovic, & Roberts, 2005; Duckitt & Harrington, 2005; Odegard, Vatten, Nilsen, Salvesen, & Austgulen, 2000; Pare et al., 2014; Steegers et al., 2010). Furthermore, recent evidence suggests that the burden of preeclampsia is not borne equally by all, with racial/ethnic minority groups reported to have higher risks than whites (Anderson, Sadler, Stewart, Fyfe, & McCowan, 2012; Breathett, Muhlestein, Foraker, & Gulati, 2014; Caughey, Stotland, Washington, & Escobar, 2005; Gong, Savitz, Stein, & Engel, 2012; Pare et al., 2014; Tanaka et al., 2007). Although disparities in preeclampsia have been shown among African Americans (Breathett et al., 2014; Caughey et al., 2005; Tanaka et al., 2007), Hispanics (Gong et al., 2012) and Maori (Anderson et al., 2012), its burden among Native Hawaiians, other Pacific Islanders and Asian ethnic groups has been inadequately studied. One retrospective study of different Pacific Islander and Asian American subgroups using a national database has shown higher rates of pregnancy-associated hypertension and eclampsia among Native Hawaiians, Samoans, Guamanian and Filipinos compared to Chinese populations (Wong et al., 2008). However, this study excluded non-Asian/Pacific Islander/Filipino patients and the data were limited to only a one-year period. Since several Asian American and Pacific Islander subgroups in Hawaii have a higher burden of risk factors for preeclampsia, including chronic hypertension, diabetes, obesity (Curb et al., 1991; Mau et al., 1997; Mau, Sinclair, Saito, Baumhofer, & Kaholokula, 2009; Moy, Sallis, & David) and other cardiovascular disease-related complications (Aluli, Reyes, & Tsark, 2007; J. Balabis, 2007), we hypothesized that these groups have higher risk of preeclampsia compared to whites.

Materials and Methods

We received approval from the University of Hawaii Institutional Review Board to conduct a retrospective study using Hawaii's Health Information Corporation (HHIC) inpatient data for

January 1995 through December 2013. HHIC data have detailed discharge data from all hospitalizations in Hawaii by all payers, and include race/ethnicity, age, sex, location of residence, insurance type, *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9) primary diagnosis, secondary diagnosis, and procedure codes.

The initial dataset included 332,083 discharges of pregnant women (age >16) who were hospitalized with a diagnosis of vaginal delivery or cesarean delivery based on the ICD-9 codes (See Appendix). Non-Hawaii residents (3,294 discharges) who gave birth in Hawaii were excluded. Since Tripler Army Medical Center does not consistently report race/ethnicity information, and the primary aim of the study was to assess the impact of race/ethnicity on the prevalence of preeclampsia, patients hospitalized at Tripler Army Medical Center (43,804 discharges) were excluded. Furthermore, a total of 13,416 discharges without race/ethnicity data were excluded, resulting in an analytic dataset that included 271,569 delivery discharges.

Outcome Measurements

The primary outcome was discharge diagnosis of preeclampsia (see Appendix). A discharge diagnosis of eclampsia was coded as “preeclampsia” for the purpose of this study since it is generally assumed that patients who had eclampsia also had preeclampsia preceding the neurological event.

Race/ethnicity

The primary purpose of the study was to compare the prevalence of preeclampsia across race/ethnic groups using HHIC race/ethnicity classifications and to investigate potential modification effects by race/ethnicity. Only one primary race/ethnicity is reported by all hospitals from patient self-report at intake, with the seven largest groups (Native Hawaiian, Japanese, Filipinos, Chinese, other Pacific Islander, other Asian, and white) accounting for 90% of the population. Mixed-race individuals who did not choose one primary racial/ethnic classification were included in the “other” group. Whites were the reference group for the comparative analyses.

Control variables

The following factors were selected a priori to be included in the multivariable models: age, insurance type (Medicaid, Department of Defense, private insurance, and other insurance), location of residence (island of Oahu vs. other Hawaiian island), multiple gestation, multiparity, chronic hypertension, pregestational diabetes, smoking, and obesity (see Appendix).

Statistical Analysis

Univariate analyses to determine the associations 1) between preeclampsia and subject characteristics, and 2) between race/ethnicity and subject characteristics were evaluated using Chi-squared or Fisher's exact tests for categorical variables, and Student *t*-tests for continuous variables. To determine whether race/ethnicity is a modifier of preeclampsia, a multivariable logistic regression was performed with the subject characteristics and their interactions with race/ethnicity. A stepwise selection method was used to determine the final

variables that were associated with preeclampsia, with consideration of the hierarchical principle (i.e., if an interaction is included in a model, all the lower level effects involved in the interaction would be included). A separate multilevel model was created to account for covariance of multiple deliveries by the same patients using a master patient identifier or hospital record identifier to link patient-level data. $P < 0.05$ was considered statistically significant. All analyses were performed in SAS 9.4.

Results

Clinical characteristics for 271,569 hospital delivery discharges (23.2% Native Hawaiian, 19.5% Filipino, 18.9% white, 11.4% Japanese, 8.2% other Pacific Islander, 5.1% other Asian, 3.4% Chinese, and 10.3% other race) are presented in Table 1. The average age of subjects was 28.4 years ($SD=6.3$). In univariate analyses, age, race/ethnicity, insurance type, multiple gestation, chronic hypertension, pregestational diabetes, smoking and obesity were associated with preeclampsia. Rates of preeclampsia were highest among Filipinos (4.6%), Native Hawaiians (4.6%), other Pacific Islanders (4.5%), and patients of other race/ethnicity (4.0%), followed by whites (2.9%), Japanese (2.8%), Chinese (2.0%), and other Asians (2.5%). Furthermore, subject characteristic comparison by race/ethnicity showed significant differences for each factor (Table 2).

The results of the multivariable logistic regression model for preeclampsia are shown in Table 3. Race/ethnicity was a significant modifier of age, multiple gestation, and obesity on preeclampsia. Using the estimates in Table 3, odds ratios for interactions were back-calculated (Table 4). For non-obese mothers of age <35 years without multiple gestation, preeclampsia rate was higher among Filipino (odds ratio [OR], 1.55, 95% confidence interval [CI], 1.43-1.67), Native Hawaiian (OR, 1.54, 95% CI, 1.43-1.66), other Pacific Islanders (OR, 1.40, 95% CI, 1.21-1.45), and other race/ethnicity (OR, 1.32, 95% CI, 1.21-1.45), but lower among Chinese (OR, 0.64, 95% CI, 0.53-0.78), compared to white. For obese mothers of age <35 years without multiple gestation, preeclampsia rate was higher among other Asian (OR, 2.73, 95% CI, 1.41-5.27) and other race/ethnicity (OR, 1.68, 95% CI, 1.09-2.58), compared to white. For non-obese mothers of age ≥ 35 years without multiple gestation, preeclampsia rates were higher among Filipino (OR, 2.26, 95% CI, 1.97-2.60), Native Hawaiians (OR, 2.31, 95% CI, 2.00-2.68), and other race/ethnicity (OR, 1.84, 95% CI, 1.54-2.20), compared to white. For obese mothers of age ≥ 35 years without multiple gestation, Filipino (OR, 1.64, 95% CI, 1.04-2.59), Native Hawaiians (OR, 1.80; 95% CI, 1.24-2.60), other Pacific Islanders, (OR, 1.68; 95% CI, 1.14-2.49), and other race/ethnicity (OR, 2.33; 95% CI, 1.48-3.68), compared to white. In addition, multiple parity (OR, 0.72; 95% CI, 0.59-0.89), pregestational diabetes (OR, 3.41; 95% CI, 3.02-3.85), chronic hypertension (OR, 5.98; 95% CI, 4.98-7.18), and smoking (OR, 1.19; 95% CI, 1.07-1.33) were independently associated with preeclampsia. A separate multilevel model was created to account for covariance of multiple deliveries by the same patients using a master patient identifier or hospital record identifier to link patient-level encounter data across hospitals statewide. The model shows very similar results in significance and in the magnitude of the statistics (results not shown).

Discussion

Using statewide administrative claims data over an 18-year period, we found that the rates of preeclampsia were higher in Native Hawaiians, other Pacific Islanders, and Filipinos but lower in Chinese and other Asians compared to whites after adjusting for many of the known risk factors for preeclampsia. Multiple gestation, pregestational diabetes, chronic hypertension, smoking and obesity were also significant preeclampsia risk factors in our model. Reasons for ethnic disparities in preeclampsia are complex, and likely involve both biological and social determinants of the disease. As suggested in prior studies (Haram, Mortensen, & Nagy, 2014; Johnson et al., 2009; Williams & Broughton Pipkin, 2011), certain ethnic groups such as Native Hawaiians, other Pacific Islanders, and Filipinos may have a higher prevalence of maternal susceptibility locus for preeclampsia compared to whites. Obesity, a modifiable risk factor, has also been strongly associated with the risk of preeclampsia. In fact, a dose-response relationship between pre-pregnancy body mass index (BMI) and preeclampsia has been shown in prior studies (Bodnar, Catov, Klebanoff, Ness, & Roberts, 2007; Bodnar et al., 2005). Furthermore, the impact of obesity on preeclampsia has been shown to be more prominent among non-Hispanic blacks compared to non-Hispanic whites (Bodnar et al., 2007), suggesting a possible race/ethnicity modification effect on a relationship between obesity and preeclampsia.

These biological factors such as obesity and diabetes that are associated with preeclampsia are also impacted by their social environment, especially poverty and racial segregation. (Black & Macinko, 2010; V. W. Chang, 2006; Krishnan, Cozier, Rosenberg, & Palmer, 2010) One social study that randomly assigned variation in neighborhood conditions showed that a move from a high level of poverty to a lower level of poverty significantly reduced the prevalence of extreme obesity and diabetes. (Ludwig et al., 2011) It is possible that a similar association between level of poverty and preeclampsia may exist, which may explain our observation. Unfortunately, due to the nature of claims database, detailed socioeconomic status was not captured and included in our model.

Interestingly, contrary to the prior studies that showed a protective effect of smoking on preeclampsia (England & Zhang, 2007), our study demonstrates that smoking is an independent risk factor for preeclampsia among our patient population. Historically, smoking has been hypothesized to reduce the risk of preeclampsia by increased placental expression of vascular endothelial growth factor (VEGF), decreased expression of soluble form of fms-like tyrosine kinase (sFlt-1), inhibition of thromboxane production, carbon monoxide-mediated inhibition of inflammation and enhanced vasodilation (England & Zhang, 2007). However, these protective roles have been shown mainly among non-Hispanic whites. In fact, a more recent study that assessed the interaction of smoking and race/ethnicity on preeclampsia demonstrated that the protective role of smoking was only seen among non-Hispanic whites and non-Hispanic American Indians; and smoking significantly increased the risk of preeclampsia among Asians and Pacific Islanders (J. J. Chang et al., 2014). The results of our study further build on the possibility that smoking may actually increase the risk of preeclampsia among Asians and Pacific Islanders.

Our study attempted to account for obesity using the discharge ICD-9 codes for obesity to assess the independent impact of race/ethnicity. However, since the prevalence of discharge diagnosis of obesity in our study was only 1.4%, which is substantially lower than the general prevalence of obesity (Aluli, 1991; Madan et al., 2012), we speculate that the vast majority of obese patients did not have this discharge diagnosis. Therefore, much of the racial/ethnic differences seen in our model may still be driven by the obesity factor particularly as rates of obesity are known to differ by race and ethnicity. Filipinos, who had the highest rates of preeclampsia in our study are also known to have higher rates of obesity than other Asian Americans (Krueger, Coleman-Minahan, & Rooks, 2014). The lower prevalence of preeclampsia among Chinese and other Asians (excluding Japanese) are consistent with prior studies (Anderson et al., 2012; Wong et al., 2008; Xiao et al., 2014), and may be related to the low prevalence of obesity among these ethnic groups (Krueger et al., 2014). Moreover, data on BMI and prior history of preeclampsia – known confounders for preeclampsia, were limited and not included in the analyses and could have accounted for some of the racial and ethnic disparities that were found in this study.

Strengths of our study include the large sample size of almost 300,000 deliveries, the detailed race/ethnicity information on this diverse, multiethnic population, and the population-based aspect of our sample that includes all deliveries in Hawaii. There are some limitations to our study, which are mostly associated with the lack of detailed clinical information as a result of using claims database. Since we could not link each individual's prior hospitalization record, we were unable to assess whether they had preeclampsia from prior pregnancies, which may have impacted our results since history of prior preeclampsia is a known risk factor. The data on gestational age at delivery and birth weight were not available, and thus the impact of preterm preeclampsia could not be assessed. The data on the duration of residence in Hawaii for each ethnic group was not available, and thus the potential impact of differences in acculturation to the western civilization could not be assessed. Since the data was limited to the state of Hawaii, our results may not be generalizable to other populations in the mainland U.S. Furthermore, the diagnostic criteria of preeclampsia has changed during the study period, which may have affected the number of reported diagnoses.

Conclusion

The rates of preeclampsia were higher in Native Hawaiians, other Pacific Islanders and Filipinos but lower in Chinese and other Asians compared to whites, depending on maternal age, obesity, and multiple gestation. For these high-risk ethnic groups, clinicians may need to provide more frequent monitoring and counseling for preeclampsia. Moreover, further study is needed to determine specific factors that are driving the disparities among these ethnic groups.

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Appendix

Definition of vaginal delivery or cesarean delivery

Vaginal delivery or cesarean delivery was defined as ICD-9 codes 641.01, 641.11, 641.21, 641.31, 641.81, 641.91, 642.01, 642.02, 642.11, 642.12, 642.21, 642.22, 642.31, 642.32, 642.41, 642.42, 642.51, 642.52, 642.61, 642.62, 642.71, 642.72, 642.91, 642.92, 643.01, 643.11, 643.21, 643.81, 643.91, 644.21, 645.11, 645.21, 646.01, 646.11, 646.12, 646.21, 646.22, 646.31, 646.41, 646.42, 646.51, 646.52, 646.61, 646.62, 646.71, 646.81, 646.82, 646.91, 647.01, 647.02, 647.11, 647.12, 647.21, 647.22, 647.31, 647.32, 647.41, 647.42, 647.51, 647.52, 647.61, 647.62, 647.81, 647.82, 647.91, 647.92, 648.01, 648.02, 648.11, 648.12, 648.21, 648.22, 648.31, 648.32, 648.41, 648.42, 648.51, 648.52, 648.61, 648.62, 648.71, 648.72, 648.81, 648.82, 648.91, 648.92, 649.01, 649.02, 649.11, 649.12, 649.21, 649.22, 649.31, 649.32, 649.41, 649.42, 649.51, 649.61, 649.62, 649.71, 649.81, 649.82, 650, 651.01, 651.11, 651.21, 651.31, 651.41, 651.51, 651.61, 651.71, 651.81, 651.91, 652.01, 652.11, 652.21, 652.31, 652.41, 652.51, 652.61, 652.71, 652.81, 652.91, 653.01, 653.11, 653.21, 653.31, 653.41, 653.51, 653.61, 653.71, 653.81, 653.91, 654.01, 654.02, 654.11, 654.12, 654.21, 654.31, 654.32, 654.41, 654.42, 654.51, 654.52, 654.61, 654.62, 654.71, 654.72, 654.81, 654.82, 654.91, 654.92, 655.01, 655.11, 655.21, 655.31, 655.41, 655.51, 655.61, 655.71, 655.81, 655.91, 656.01, 656.21, 656.31, 656.41, 656.51, 656.61, 656.71, 656.81, 656.91, 657.01, 658.01, 658.11, 658.21, 658.31, 658.41, 658.81, 658.91, 659.01, 659.11, 659.21, 659.31, 659.41, 659.51, 659.61, 659.71, 659.81, 659.91, 660.01, 660.11, 660.21, 660.31, 660.41, 660.51, 660.71, 660.81, 660.91, 661.01, 661.11, 661.21, 661.31, 661.41, 661.91, 662.01, 662.11, 662.21, 662.31, 663.01, 663.11, 663.21, 663.31, 663.41, 663.51, 663.61, 663.81, 663.91, 664.01, 664.11, 664.21, 664.31, 664.41, 664.51, 664.61, 664.81, 664.91, 665.01, 665.11, 665.22, 665.31, 665.51, 665.61, 665.71, 665.72, 665.81, 665.82, 665.91, 665.92, 666.02, 666.12, 666.22, 666.32, 667.02, 667.12, 668.01, 668.02, 668.11, 668.12, 668.21, 668.22, 668.81, 668.82, 668.91, 668.92, 669.01, 669.02, 669.11, 669.12, 669.21, 669.22, 669.32, 669.41, 669.42, 669.51, 669.61, 669.71, 669.81, 669.82, 669.91, 669.92, 670.02, 670.12, 670.22, 670.32, 670.82, 671.01, 671.02, 671.11, 671.12, 671.21, 671.22, 671.31, 671.42, 671.51, 671.52, 671.81, 671.82, 671.91, 671.92, 672.02, 673.01, 673.02, 673.11, 673.12, 673.21, 673.22, 673.31, 673.32, 673.81, 673.82, 674.01, 674.02, 674.12, 674.22, 674.32, 674.42, 674.51, 674.52, 674.82, 674.92, 675.01, 675.02, 675.11, 675.12, 675.21, 675.22, 675.81, 675.82, 675.91, 675.92, 676.01, 676.02, 676.11, 676.12, 676.31, 676.32, 676.41, 676.42, 676.51, 676.52, 676.61, 676.62, 676.81, 676.82, 676.91, 676.92, 678.01, 678.11, 679.01, 679.02, 679.11, 679.12, v27.0, v27.1, v27.2, v27.3, v27.4, v27.5, v27.6, v27.7, v27.9.

Definition of preeclampsia or eclampsia

Preeclampsia or eclampsia was defined as ICD-9 codes 642.40, 642.41, 642.42, 642.43, 642.44, 642.50, 642.51, 642.53, 642.54, 642.60, 642.61, 642.63, 642.64, 642.70, 642.71, 642.73, 642.74.

Definition of multiple gestation

Multiple gestation was defined as ICD-9 codes 651.70, 651.71, 651.73, 651.80, 651.83, 651.90, 651.91, 651.93, 652.60, 652.61, 652.63, V91.90, V91.91, V91.92, V91.99.

Definition of multiparity

Multiparity was defined as ICD-9 codes 659.40, 659.41, 659.43, V23.3, V61.5.

Definition of chronic hypertension

Chronic hypertension was defined as ICD-9 codes 401.00, 401.10, 401.90, 405.01, 405.09, 405.11, 405.19, 405.91, 405.99, 642.00, 642.03, 642.10, 642.13, 642.20, 642.21, 642.22, 642.24.

Definition of pregestational diabetes

Pregestational diabetes was defined as ICD-9 codes 249.00, 249.01, 249.10, 249.11, 249.20, 249.21, 249.30, 249.31, 249.40, 249.41, 249.50, 249.51, 249.60, 249.61, 249.70, 249.71, 249.80, 249.81, 249.90, 249.91, 250.00, 250.01, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33, 250.41, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93, 648.03.

Definition of smoking

Smoking was defined as ICD-9 codes 305.10, 649.00, 649.01, 649.02, 649.03, 649.04, V15.82.

Definition of obesity

Obesity was defined as ICD-9 codes 278.0, 278.1, 278.2, 278.3, 278.4, 278.8.

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Significance

What is already known on this subject?

Minorities such as African Americans have higher incidence of preeclampsia compared to non-Hispanic whites. However, the burden of preeclampsia among Native Hawaiians, other Pacific Islanders, and Asian Americans in Hawaii has not been adequately studied.

What this study adds?

This study showed that the rates of preeclampsia were higher in Native Hawaiians, other Pacific Islanders, Filipinos, and other Asians but lower in Chinese compared to whites, with respect to age, obesity, and multiple gestation. The findings of this study further add to the growing health concerns among Native Hawaiians and other Pacific Islanders in Hawaii.

Table 1
Subject Characteristics

Variable	Total (N = 271,569)	Preeclampsia, n (%)		p-value
		No (N = 261,248)	Yes (N = 10,321)	
Age				<0.001
<35 years	221,543 (81.6%)	213,525 (96.4%)	8,018 (3.6%)	
≥35 years	50,026 (18.4%)	47,723 (95.4%)	2,303 (4.6%)	
Maternal Race/Ethnicity				<0.001
Chinese	9,289 (3.4%)	9,103 (98.0%)	186 (2.0%)	
Filipino	53,122 (19.5%)	50,657 (95.4%)	2,465 (4.6%)	
Native Hawaiian	62,933 (23.2%)	60,031 (95.4%)	2,902 (4.6%)	
Japanese	30,992 (11.4%)	30,134 (97.2%)	858 (2.8%)	
Other Asian	13,853 (5.1%)	13,506 (97.5%)	347 (2.5%)	
Other Pacific Islanders	22,245 (8.2%)	21,247 (95.5%)	998 (4.5%)	
Other	27,876 (10.3%)	26,772 (96.0%)	1,104 (4.0%)	
White	51,259 (18.9%)	49,798 (97.1%)	1,461 (2.9%)	
Insurance Type				<0.001
Department of Defense	4,675 (1.7%)	4,521 (96.7%)	154 (3.3%)	
Medicaid	91,661 (33.8%)	87,903 (95.9%)	3,781 (4.1%)	
Other Insurance	6,234 (2.3%)	6,042 (96.9%)	192 (3.1%)	
Private	168,999 (62.2%)	162,782 (96.3%)	6,217 (3.7%)	
Location of Residence				0.209
Island of Oahu (Urban)	183,881 (67.7%)	176,834 (96.2%)	7,047 (3.8%)	
Other Hawaiian Islands (Rural)	87,688 (32.3%)	84,414 (96.3%)	3,274 (3.7%)	
Multiple Gestation				<0.001
No	270,122 (99.5%)	259,952 (96.2%)	10,170 (3.8%)	
Yes	1,447 (0.5%)	1,296 (89.4%)	151 (10.6%)	
Multiparity				0.266
No	269,060 (99.1%)	258,833 (96.2%)	10,227 (3.8%)	
Yes	2,509 (0.9%)	2,415 (96.3%)	94 (3.8%)	
Chronic Hypertension				<0.001
No	270,868 (99.7%)	260,712 (96.3%)	10,156 (3.7%)	
Yes	701 (0.3%)	536 (76.5%)	165 (23.5%)	
Pregestational Diabetes				<0.001
No	269,289 (99.2%)	259,324 (96.3%)	9,965 (3.7%)	
Yes	2,280 (0.8%)	1,924 (84.4%)	356 (15.6%)	
Smoking				<0.001
No	264,887 (97.5%)	254,928 (96.2%)	9,959 (3.8%)	
Yes	6,682 (2.5%)	6,320 (94.6%)	362 (5.4%)	
Obesity				<0.001

Variable	Total (N = 271,569)	Preeclampsia, n (%)		p-value
		No (N = 261,248)	Yes (N = 10,321)	
No	267,776 (98.6%)	257,957 (96.3%)	9,819 (3.7%)	
Yes	3,793 (1.4%)	3,291 (86.8%)	502 (13.2%)	
Period with Different Diagnostic Criteria for Preeclampsia				<0.001
Before year 2000	68,698 (25.3%)	66,249 (96.4%)	2,449 (3.6%)	
Between year 2000 and year 2013 November	200,271 (74.7%)	192,512 (96.1%)	7,759 (3.9%)	
After 2013 November	2,600 (1.0%)	2,487 (95.7%)	113 (4.4%)	

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Table 2

Subject Characteristics by Maternal Race/Ethnicity

Variable	Total (N = 271,569)	Maternal Race/Ethnicity, n (%)								p-value	
		Chinese (n=9,289)	Filipino (n=53,122)	Native Hawaiian (n=62,933)	Japanese (n=30,992)	Other Asian (n=13,853)	Other Pacific Islanders (n=22,245)	Other (n=27,876)	White (N = 51,259)		
Age											<0.001
<35 years	221,543 (81.6%)	6,345 (68.3%)	43,774 (82.4%)	56,520 (89.8%)	20,305 (65.5%)	10,553 (76.2%)	19,791 (89.0%)	24,123 (86.5%)	40,132 (78.3%)		
35 years	50,026 (18.4%)	2,944 (31.7%)	9,348 (17.6%)	6,413 (10.2%)	10,687 (34.5%)	3,300 (23.8%)	2,454 (11.0%)	3,753 (13.5%)	11,127 (21.7%)		
Insurance Type											<0.001
Department of Defense	4,675 (1.7%)	49 (0.5%)	491 (0.9%)	584 (0.9%)	176 (0.6%)	134 (1.0%)	166 (0.8%)	753 (2.7%)	2,322 (4.5%)		
Medicaid	91,661 (33.8%)	1,539 (16.6%)	13,605 (25.6%)	30,445 (48.4%)	2,857 (9.2%)	3,521 (25.4%)	14,775 (66.4%)	10,827 (38.8%)	14,092 (27.5%)		
Other Insurance	6,234 (2.3%)	262 (2.8%)	796 (1.5%)	672 (1.1%)	848 (2.7%)	544 (3.9%)	1,101 (5.0%)	1,092 (3.9%)	919 (1.8%)		
Private	168,999 (62.2%)	7,439 (80.1%)	38,230 (72.0%)	31,232 (49.6%)	27,111 (87.5%)	9,654 (69.7%)	6,203 (27.9%)	15,204 (54.5%)	33,926 (66.2%)		
Location of Residence											<0.001
Island of Oahu	183,881 (67.7%)	8,586 (92.4%)	38,435 (72.4%)	36,734 (58.4%)	25,463 (82.2%)	12,433 (89.8%)	17,712 (79.6%)	18,752 (67.3%)	25,766 (50.3%)		
Other Hawaiian Islands	87,688 (32.3%)	703 (7.6%)	14,687 (27.6%)	26,199 (41.6%)	5,529 (17.8%)	1,420 (10.3%)	4,533 (20.4%)	9,124 (32.7%)	25,493 (49.7%)		
Multiple Gestation											<0.001
No	270,122 (99.5%)	9,234 (99.4%)	52,908 (99.6%)	62,622 (99.5%)	30,764 (99.3%)	13,796 (99.6%)	22,105 (99.4%)	27,715 (99.4%)	50,978 (99.5%)		
Yes	1,447 (0.5%)	55 (0.6%)	214 (0.4%)	311 (0.5%)	228 (0.7%)	57 (0.4%)	140 (0.6%)	161 (0.6%)	281 (0.6%)		
Multiparity											<0.001
No	269,060 (99.1%)	9,277 (99.9%)	52,813 (99.4%)	62,106 (98.7%)	30,922 (99.8%)	13,778 (99.5%)	21,529 (96.8%)	27,631 (99.1%)	51,004 (99.5%)		
Yes	2,509 (0.9%)	12 (0.1%)	309 (0.6%)	827 (1.3%)	70 (0.2%)	75 (0.5%)	716 (3.2%)	245 (0.9%)	255 (0.5%)		
Chronic Hypertension											<0.001
No	270,868 (99.7%)	9,276 (99.9%)	52,950 (99.7%)	62,740 (99.7%)	30,900 (99.7%)	13,832 (99.8%)	22,201 (99.8%)	27,825 (99.8%)	51,144 (99.8%)		
Yes	701 (0.3%)	13 (0.1%)	172 (0.3%)	193 (0.3%)	92 (0.3%)	21 (0.2%)	44 (0.2%)	51 (0.2%)	115 (0.2%)		
Pregestational Diabetes											<0.001
No	269,289 (99.2%)	9,242 (99.5%)	52,645 (99.1%)	62,273 (99.0%)	30,767 (99.3%)	13,793 (99.6%)	21,879 (98.4%)	27,657 (99.2%)	51,033 (99.6%)		
Yes	2,280 (0.8%)	47 (0.5%)	477 (0.9%)	660 (1.0%)	225 (0.7%)	60 (0.4%)	366 (1.7%)	219 (0.8%)	226 (0.4%)		
Smoking											<0.001
No	264,887 (97.5%)	9,181 (98.8%)	52,128 (98.1%)	60,647 (96.4%)	30,459 (98.3%)	13,606 (98.2%)	21,334 (95.9%)	27,295 (97.9%)	50,237 (98.0%)		

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Variable	Total (N = 271,569)	Maternal Race/Ethnicity, n (%)								p-value
		Chinese (n=9,289)	Filipino (n=53,122)	Native Hawaiian (n=62,933)	Japanese (n=30,992)	Other Asian (n=13,853)	Other Pacific Islanders (n=22,245)	Other (n=27,876)	White (N = 51,259)	
Yes	6,682 (2.5%)	108 (1.2%)	994 (1.9%)	2,286 (3.6%)	533 (1.7%)	247 (1.8%)	911 (4.1%)	581 (2.1%)	1,022 (2.0%)	<0.001
Obesity										
No	267,776 (98.6%)	9,239 (99.6%)	52,783 (99.4%)	61,608 (97.9%)	30,884 (99.7%)	13,785 (99.5%)	21,108 (94.9%)	27,552 (98.8%)	50,807 (99.1%)	
Yes	3,793 (1.4%)	40 (0.4%)	339 (0.6%)	1,325 (2.1%)	108 (0.4%)	68 (0.5%)	1,137 (5.1%)	324 (1.2%)	452 (0.9%)	
Period with Different Diagnostic Criteria for Preeclampsia										<0.001
Before year 2000	68,698 (25.3%)	2,736 (29.4%)	13,637 (25.7%)	15,758 (25.0%)	8,435 (27.2%)	3,977 (28.7%)	3,703 (16.7%)	7,004 (25.1%)	13,448 (26.2%)	
Between year 2000 and year 2013	200,271 (74.7%)	6,462 (69.6%)	38,937 (73.3%)	46,576 (74.0%)	22,301 (72.0%)	9,770 (70.5%)	18,250 (82.0%)	20,705 (74.3%)	37,270 (72.7%)	
After year 2013	2,600 (1.0%)	91 (1.0%)	548 (1.0%)	599 (1.0%)	256 (0.8%)	106 (0.8%)	282 (1.3%)	167 (0.6%)	541 (1.1%)	

Table 3
Multivariable Logistic Regression Model

Variable	Estimate	Standard Error	p-value
Intercept	-3.063	0.031	<0.001
Age			
<35 years	Ref		
≥35 years	0.053	0.063	0.405
Maternal Race/Ethnicity			
White	Ref		
Chinese	-0.448	0.101	<0.001
Filipino	0.436	0.039	<0.001
Native Hawaiian	0.431	0.038	<0.001
Japanese	-0.097	0.055	0.077
Other Asian	-0.126	0.071	0.076
Other Pacific Islanders	0.334	0.049	<0.001
Other	0.280	0.047	<0.001
Multiparity	-0.324	0.108	0.003
Multiple Gestation (MG)	1.484	0.191	<0.001
Pregestational Diabetes	1.227	0.062	<0.001
Chronic Hypertension	1.788	0.094	<0.001
Smoking	0.175	0.057	0.002
Obesity	1.286	0.160	<0.001
Maternal Race/Ethnicity*Age			
White at Age ≥35	Ref		
Chinese at Age ≥35	0.252	0.166	0.128
Filipino at Age ≥35	0.381	0.080	<0.001
Native Hawaiian at Age ≥35	0.407	0.083	<0.001
Japanese at Age ≥35	0.134	0.096	0.162
Other Asian at Age ≥35	-0.062	0.143	0.666
Other Pacific Islanders at Age ≥35	0.444	0.108	<0.001
Other at Age ≥35	0.330	0.102	0.001
Maternal Race/Ethnicity*MG			
White with MG	Ref		
Chinese with MG	-0.473	0.630	0.453
Filipino with MG	-0.564	0.288	0.051
Native Hawaiian with MG	-0.750	0.275	0.006
Japanese with MG	0.165	0.277	0.551
Other Asian with MG	-0.106	0.509	0.835
Other Pacific Islanders with MG	-0.808	0.363	0.026
Other with MG	-0.597	0.335	0.074

Variable	Estimate	Standard Error	p-value
Maternal Race/Ethnicity*Obesity			
Obese White	Ref		
Obese Chinese	0.446	0.523	0.394
Obese Filipino	-0.321	0.228	0.159
Obese Native Hawaiian	-0.253	0.181	0.162
Obese Japanese	-0.023	0.346	0.940
Obese Other Asian	1.130	0.340	<0.001
Obese Other Pacific Islanders	-0.258	0.188	0.171
Other	0.238	0.221	0.282

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Table 4
Odds Ratio and 95% Confidence Interval

(A) Modification Effect: Race/Ethnicity by Age, Multiple Gestation, and Obesity				
Age	Multiple Gestation	Obesity	Maternal Race/Ethnicity	Odds Ratio (95% CI)
<35	No	No	Chinese vs. White	0.64 (0.53-0.78)*
			Filipino vs. White	1.55 (1.43-1.67)*
			Native Hawaiian vs. White	1.54 (1.43-1.66)*
			Japanese vs. White	0.91 (0.82-1.01)
			Other Asian vs. White	0.88 (0.77-1.01)
			Other Pacific Islanders vs. White	1.40 (1.27-1.54)*
			Other Race vs. White	1.32 (1.21-1.45)*
		Yes	Chinese vs. White	1.00 (0.36-2.76)
			Filipino vs. White	1.12 (0.72-1.75)
			Native Hawaiian vs. White	1.20 (0.84-1.70)
			Japanese vs. White	0.89 (0.45-1.74)
			Other Asian vs. White	2.73 (1.41-5.27)*
			Other Pacific Islanders vs. White	1.08 (0.75-1.55)
			Other Race vs. White	1.68 (1.09-2.58)*
	Yes	No	Chinese vs. White	0.40 (0.12-1.37)
			Filipino vs. White	0.88 (0.50-1.55)
			Native Hawaiian vs. White	0.73 (0.43-1.24)
			Japanese vs. White	1.07 (0.62-1.85)
			Other Asian vs. White	0.79 (0.23-2.15)
			Other Pacific Islanders vs. White	0.62 (0.31-1.27)
			Other Race vs. White	0.73 (0.38-1.40)
Yes		Chinese vs. White	0.62 (0.13-3.08)	
		Filipino vs. White	0.64 (0.31-1.30)	
		Native Hawaiian vs. White	0.56 (0.30-1.07)	
		Japanese vs. White	1.04 (0.44-2.46)	
		Other Asian vs. White	2.46 (0.74-8.11)	
		Other Pacific Islanders vs. White	0.48 (0.22-1.06)	
		Other Race vs. White	0.92 (0.43-2.01)	
35	No	No	Chinese vs. White	0.82 (0.63-1.07)
			Filipino vs. White	2.26 (1.97-2.60)*
			Native Hawaiian vs. White	2.31 (2.00-2.68)*
			Japanese vs. White	1.04 (0.89-1.21)
			Other Asian vs. White	0.83 (0.64-1.06)
			Other Pacific Islanders vs. White	2.18 (1.79-2.64)*
			Other Race vs. White	1.84 (1.54-2.20)*
		Yes	Chinese vs. White	1.28 (0.46-3.63)

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(A) Modification Effect: Race/Ethnicity by Age, Multiple Gestation, and Obesity				
<i>Age</i>	<i>Multiple Gestation</i>	<i>Obesity</i>	<i>Maternal Race/Ethnicity</i>	<i>Odds Ratio (95% CI)</i>
			Filipino vs. White	1.64 (1.04-2.59)*
			Native Hawaiian vs. White	1.80 (1.24-2.60)*
			Japanese vs. White	1.01 (0.51-2.01)
			Other Asian vs. White	2.57 (1.29-5.12)*
			Other Pacific Islanders vs. White	1.68 (1.14-2.49)*
			Other Race vs. White	2.33 (1.48-3.68)*
	Yes	No	Chinese vs. White	0.51 (0.15-1.75)
			Filipino vs. White	1.29 (0.73-2.27)
			Native Hawaiian vs. White	1.09 (0.63-1.88)
			Japanese vs. White	1.22 (0.71-2.11)
			Other Asian vs. White	0.75 (0.27-2.04)
			Other Pacific Islanders vs. White	0.97 (0.47-2.00)
		Yes	Chinese vs. White	0.80 (0.16-3.97)
			Filipino vs. White	0.93 (0.46-1.91)
			Native Hawaiian vs. White	0.85 (0.45-1.61)
			Japanese vs. White	1.19 (0.51-2.82)
			Other Asian vs. White	2.31 (0.69-7.69)
			Other Pacific Islanders vs. White	0.75 (0.34-1.67)
Other Race vs. White	1.28 (0.59-2.82)			

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(B) Modification Effect: Age, Multiple Gestation, and Obesity within Race/Ethnicity			
<i>Maternal Race/Ethnicity</i>	Odds Ratio (95% CI)		
	<i>Age</i>	<i>Multiple Gestation</i>	<i>Obesity</i>
	35 vs. <35	Yes vs. No	Yes vs. No
Chinese	1.36 (1.01-1.83)*	2.75 (0.85-8.91)	5.65 (2.13-14.99)*
Filipino	1.54 (1.40-1.70)*	2.51 (1.64-3.83)*	2.63 (1.91-3.61)*
Native Hawaiian	1.58 (1.43-1.76)*	2.08 (1.41-3.06)*	2.81 (2.38-3.32)*
Japanese	1.21 (1.05-1.39)*	5.20 (3.51-7.71)*	3.53 (1.93-6.44)*
Other Asian	0.99 (0.77-1.27)	3.97 (1.57-10.00)*	11.20 (6.22-20.17)*
Other Pacific Islanders	1.64 (1.39-1.95)*	1.97 (1.07-3.60)*	2.80 (2.30-3.40)*
Other Race	1.47 (1.25-1.72)*	2.43 (1.42-4.16)*	4.59 (3.40-6.20)*
White	1.05 (0.93-1.19)	4.41 (3.03-6.41)*	3.62 (2.64-6.20)*

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(C) Main Effect	
<i>Variable</i>	<i>Odds Ratio (95% CI)</i>
Multiparity	0.72 (0.59-0.89)*
Pregestational Diabetes	3.41 (3.02-3.85)*
Chronic Hypertension	5.98 (4.98-7.18)*

Smoking	1.19 (1.07-1.33)*
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* P <0.05

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