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Differences in Thrombotic Risk Factors in Black and White Women with Adverse Pregnancy Outcome☆

Claire S. Philipp [a,*], Ambarina S. Faiz [a], Michele G. Beckman [b], Althea Grant [b], Paula L. Bockenstedt [c], John A. Heit [d], Andra H. James [e,1], Roshni Kulkarni [f], Marilyn J. Manco-Johnson [g], Stephan Moll [h], Thomas L. Ortel [i]

[a] Department of Medicine, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA
[b] Division of Blood Disorders, Centers for Disease Control and Prevention, Atlanta, GA, USA
[c] Department of Medicine, University of Michigan, Ann Arbor, MI, USA
[d] Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA
[e] Department of Obstetrics and Gynecology, Duke University, Durham, NC, USA
[f] Department of Pediatrics and Human Development, Michigan State University, East Lansing, MI, USA
[g] Department of Pediatrics, University of Colorado, Denver and the Children's Hospital, Aurora, CO, USA
[h] Department of Medicine, University of North Carolina, Chapel Hill, NC, USA
[i] Departments of Medicine and Pathology, Duke University, Durham, NC, USA

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ABSTRACT

Introduction: Black women have an increased risk of adverse pregnancy outcomes and the characteristics of thrombotic risk factors in this population are unknown. The objective of this study was to examine the racial differences in thrombotic risk factors among women with adverse pregnancy outcomes.
Methods: Uniform data were collected in women with adverse pregnancy outcomes (pregnancy losses, intrauterine growth restriction (IUGR), prematurity, placental abruption and preeclampsia) referred to Thrombosis Network Centers funded by the Centers for Disease Control and Prevention (CDC).
Results: Among 343 white and 66 black women seen for adverse pregnancy outcomes, protein S and antithrombin deficiencies were more common in black women. The prevalence of diagnosed thrombophilia was higher among whites compared to blacks largely due to Factor V Leiden mutation. The prevalence of a personal history of venous thromboembolism (VTE) did not differ significantly by race. A family history of VTE, thrombophilia, and stroke or myocardial infarction (MI) was higher among whites. Black women had a higher body mass index, and a higher prevalence of hypertension, while the prevalence of sickle cell disease was approximately 27 fold higher compared to the general US black population.
Conclusions: Thrombotic risk factors differ significantly in white and black women with adverse pregnancy outcomes. Such differences highlight the importance of considering race separately when assessing thrombotic risk factors for adverse pregnancy outcomes.

Introduction

There are significant disparities in rates of adverse pregnancy outcomes between black and white women [1]. In the US, 69% of pregnancies among white women end in live birth compared to 49% of pregnancies in black women [1], and black women have increased rates of fetal loss compared to white women (11.13 vs 4.79 per 1000 live births) [2]. A multicenter US study limited to women with early access to prenatal care reported an approximately 3-4 fold increased risk of both early and late fetal demise in black women compared to white women after adjusting for multiple maternal and socioeconomic characteristics [3]. In addition, significantly higher rates of intrauterine growth restriction, preeclampsia, preterm birth, and placental abruption have been found in black women compared to white women [2,3]. Despite improvements in obstetric care, major racial disparities in adverse pregnancy outcomes persist and remain unexplained.

Thrombotic risk factors have been associated with pregnancy complications [4–8]. Many previous studies have found an association between inherited thrombophilia and adverse pregnancy outcomes, however there has been wide variability in the strength of the association and some studies have not found a relationship [4,6–12]. Despite significant racial disparities in rates of adverse pregnancy outcomes, most studies examining the relationship of thrombotic risk factors in women with adverse pregnancy outcomes have been performed in white populations, and have focused on Factor V Leiden and

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* Corresponding author at: Division of Hematology, MEB Rm 378, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ 08903. Tel.: +1 732 235 7682.
E-mail address: philipp@rutgers.edu (C.S. Philipp).
[1] Current affiliation: University of Virginia, Charlottesville, Virginia.

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prothrombin gene mutations [9–12], thrombotic risk factors known to be less prevalent among black populations [13,14]. There is very limited information on thrombophilia and other thrombotic risk factors in black women with adverse pregnancy outcomes. The objective of this study was to compare the characteristics of thrombotic risk factors among black and white women with adverse pregnancy outcomes receiving care and participating in a multi-site registry at US Thrombosis Network Centers.

Methods

Consecutive patients seen in consultation at any of the Thrombosis and Hemostasis Research and Prevention Network Centers, funded by the Centers for Disease Control and Prevention (CDC), were approached for participation in a patient registry regardless of the reason for their visit, age, sex, or race. After obtaining informed consent, a standardized data collection form was completed by center staff during initial and subsequent visits. Uniform data were prospectively collected from August 2003 to March 2011 and were entered into a web-based registry housed at the CDC, Division of Blood Disorders. De-identified data were submitted by unique patient study identification number. Institutional Review Board approval was obtained at each of the network centers and the CDC and continuing approval obtained annually. Information for the patient registry was collected by network center medical providers at the time of the visit and included demographic and clinical characteristics, concurrent medical conditions, family history, laboratory and radiologic tests, diagnosis, and treatments prescribed. The CDC funded Thrombosis Network Centers and registry have been previously described [15–17].

To examine the prevalence of thrombotic risk factors in women with adverse pregnancy outcomes, we searched the patient registry for women age 15 years and older at enrollment who had been referred to one of the Thrombosis and Hemostasis Network Centers for pre-pregnancy, pregnancy, or postpartum consultation. From this group of women, we included only women seen for adverse pregnancy outcomes. We further restricted analysis to women of black or white race and compared thrombotic and clinical characteristics between the two racial groups.

Adverse pregnancy outcomes were defined as a documented history of pregnancy loss or losses, intrauterine growth restriction (IUGR), preterm delivery, placental abruption and/or preeclampsia. Race was self-identified. Those who selected more than one race were categorized as “other” race and included in the “other” race subgroup. In addition to individuals selecting more than one race, the “other” race category also included Asians, American Indian, Alaskan native, and Pacific Islanders. The “other” racial category was not included in the data analyzed.

The registry included a history of medical comorbidites including diabetes, hypertension, sickle cell disease, cancer, myocardial infarction and stroke for each woman. The history and clinical presentation of diagnosed thromboembolic events, locations of thrombi, and associated risks such as surgery, trauma, contraceptive use, and hormonal replacement therapy were also collected. Self-reported family histories of thromboembolism, adverse pregnancy outcomes, and diagnosed thrombophilia were also obtained. Medical comorbidities, thromboembolic events, associated thrombotic risk, and family history were compared between the two racial groups.

For this study, thrombophilia was defined as factor V Leiden or prothrombin G20210A mutations, deficiency of antithrombin, protein C, or protein S, or antiphospholipid antibody syndrome (APS) at enrollment or by evaluation by the Center. For most diagnoses made prior to evaluation at the center, the thrombophilia diagnosis was confirmed by testing performed on-site at the network centers. The diagnosis of APS was based on the Sapporo classification [18].

A history of venous thromboembolism (VTE) was defined as VTE diagnosed by venography, angiography, duplex ultrasonography, impedence plethysmography, computed tomographic venography or angiography, MRI, or high probability ventilation perfusion scan.

The prevalence of *a.priori* selected demographic and clinical characteristics were calculated and compared between blacks and whites. For categorical variables Pearson’s chi-square test was used and in the case of small cell sizes (<5) Fisher’s exact p values were reported. The prevalence of protein S deficiency was also evaluated in the subgroup of women who were not known to be pregnant at the time of study enrollment. Mean values were computed for the continuous variables of age and body mass index (BMI) at the time of enrollment and differences between the racial groups were assessed using Student’s t-test. A p-value < 0.05 was considered statistically significant for the analyses. The data were analyzed using SAS statistical package version 9.2(SAS Institute, Cary, NC).

Results

Between August 2003 and March 2011, 833 women, (631 white, 152 black, and 50 of other or missing race) were referred to a participating Network Center for pregnancy, pre-pregnancy, or postpartum consultation or management and enrolled into the patient registry. The mean age at enrollment was 34.8 ± 10.5 years. Of these 833 women, 434 were seen for a history of adverse pregnancy outcome (343 white, 66 black, and 25 of other or missing races). The adverse pregnancy outcomes included pregnancy loss or recurrent losses, IUGR, preterm delivery, preeclampsia, and placental abruption.

Among the 409 women of black or white race with an adverse pregnancy outcome, the mean age at enrollment was 39.1 ± 11.8 years and 33.8 ± 10.4 years for white and black women respectively ($p < 0.01$). The average body mass index (BMI) at enrollment was higher (31.9 ± 9.6 vs 29.1 ± 11.1 kg/m^2, $p = 0.07$) in black women and the prevalence of non-pregnant BMI ≥ 25 was significantly higher in black women than white women (86.2% vs 63.4%, $p = 0.01$) (Table 1). The adverse pregnancy outcomes did not differ significantly by race except for second trimester loss, which was more common among black women (33.3% vs 21.9%, $p = 0.05$) (Table 2).

The prevalence of diagnosed thrombophilia differed by race. Overall, thrombophilia was more common in white women with adverse pregnancy outcomes compared to black women (44% vs 30.3%, $p = 0.04$) (Table 3), although this difference was primarily due to the difference in factor V Leiden mutation (19% vs 3%, $p < 0.01$). However, protein S deficiency was significantly more common in black women (15.2 % vs 5.8 %, $p = 0.02$) (Table 3). When assessed among the subgroup of women who were not pregnant at study enrollment (252 white and 32 black), protein S deficiency was still more common in black women but the difference did not reach statistical significance (13.5 % vs 5.5 %, $p = 0.08$). None of the women with protein S deficiency had sickle cell disease, renal disease, or HIV. Antithrombin deficiency was also more common among black women (6% vs 1.5%, $p = 0.04$). There were no racial differences in the frequency of laboratory testing for protein S or antithrombin.

Table 1
Characteristics of Study Population with Adverse Pregnancy Outcomes by Race(N = 409).

Characteristics	White (N = 343)	Black (N = 66)	p-value
Age* (in years) mean ± SD	39.1 ± 11.8	33.8 ± 10.4	<0.01
BMI* (kg/m^2) mean ± SD	29.1 ± 11.1	31.9 ± 9.6	0.07
Smoking* N (%)	53 (15.5)	9 (13.6)	0.71
BMI** non-pregnant N (%)	(N = 246)	(N = 29)	
<25	90 (36.6)	4 (13.8)	0.01
≥25	156 (63.4)	25 (86.2)	

* At enrollment into registry.
** N is different because of missing values.