

Tracking the Development of Cerebrovascular Risk Factors Following Pregnancy With Preeclampsia

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Objective: To evaluate the development and management of cerebrovascular risk factors following a pregnancy with preeclampsia. **Methods:** This is a retrospective chart review including women diagnosed with preeclampsia between 2012 and 2013 with later encounters within 2014-2016. For each subject that met inclusion criteria, the development of cerebrovascular risk factors was determined using ICD codes within the 2014-2016 electronic medical record (EMR). For subjects who developed risk factors, current treatment was determined from the EMR. Demographic data was also documented. Differences in the development and treatment of risk factors were compared among racial groups and age. Descriptive statistics were calculated using SAS statistical software. **Results:** Compared to prepregnancy health status, the incidence of hypertension increased by 1.7 times ($P < .05$), hyperlipidemia increased by 4.5 ($P < .05$), migraines increased by 2.2 ($P < .05$), and diabetes mellitus increased by 2 ($P < .05$) after a pregnancy with preeclampsia. Black non-Hispanics had highest rates of hypertension, obesity, and migraines (20.5%, 9.1%, and 6.8%, respectively.) Of hypertensives, 73.6% (42/57) were prescribed medication. Of diabetics, 88.9% (16/18) were prescribed medication. No patients with hyperlipidemia were prescribed a statin. Black non-Hispanics had higher rates of risk factor management (74.3% of hypertensives and 100% of diabetics treated) than white Hispanics (55% and 77.8%, respectively). **Conclusions:** This study shows a significant increased risk of the development of cerebrovascular risk factors such as hypertension, hyperlipidemia, migraines, and diabetes following a diagnosis of preeclampsia. Opportunities exist for the early treatment of these risk factors, which could reduce the long-term rate of stroke in these women

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Introduction

While improved risk factor modification has led to an overall decrease in stroke mortality in the United States, we are seeing less significant progress within younger adults. In fact, there is evidence that the incidence of stroke is actually increasing among this age group. A study in 2011 reported that hospitalization rates due to acute stroke were increasing in adults age 15-44.¹ This increase stroke burden in young adults may be due to earlier appearance of risk factors such as obesity, diabetes, hypertension, and hyperlipidemia. Prompt identification and management of risk factors is considered the primary treatment strategy for reducing stroke related morbidity and mortality, and it is essential this be done in younger adults.

Preeclampsia is a multisystem disease defined as the onset of hypertension and either proteinuria or end-organ dysfunction after 20 weeks of gestation. After pregnancy, women with a history of preeclampsia have a higher lifetime risk for hypertension, cardiovascular disease, and cerebrovascular disease.² It has been suggested that cerebrovascular disease and preeclampsia are expressions of the same disease process, as they share the same risk factors (high maternal age, diabetes mellitus, obesity, and renal disease).³ There may also be an adverse cardiovascular phenotype which predisposes mothers to hypertensive complications of pregnancy.⁴

Tracking the development of risk factors for vascular disease after preeclampsia is thus necessary to address the increase incidence in stroke in young adults. Between 5% and 8% of women are affected by preeclampsia during their pregnancy.⁵ The relationship between hypertensive disorders of pregnancy and risk of stroke has been quantified in large retrospective studies, mostly in northern European populations.⁶ It is not well established how the risk is distributed in diverse North American settings. This study was designed to identify the short-term development of risk factors for stroke in an urban group of women who experienced preeclampsia and did not have major vascular risk factors before pregnancy. We sought to track how these risk factors were managed medically following the pregnancy.

Materials and Methods

This study identified female patients diagnosed with preeclampsia at Jackson Memorial Hospital (JMH) between January 2012 and December 2013 who also had subsequent follow up within the Jackson Health System between January 2014 and December 2016. Inclusion criteria for the study were adult female of age over 18 years old of any racial background and socioeconomic status diagnosed with preeclampsia during pregnancy and no previous diagnosis of stroke. Patients under 18 years old were excluded from the study. Diagnostic criteria for preeclampsia as outlined by the American College of Obstetricians and Gynecologists were used to reconfirm preeclampsia diagnoses made in the patients' electronic health records.⁷ The development of hypertension, hyperlipidemia, migraines, obesity, and diabetes mellitus—all risk factors for cerebrovascular events, within January 2014 and December 2016 were tracked for all subjects. Hypertension was defined as higher than equal to 140/90 mm Hg at more than 2 physician visits. It was noted whether these comorbidities were managed appropriately with medications (specifically, an antihypertensive medication for hypertension, a statin for hyperlipidemia, and a glucose-lowering agent for diabetes mellitus). Following the 2013 American Heart Association/American College of Cardiology Lifestyle Management Guideline for statin use, we considered the need for a statin among patients

who had low-density lipoprotein cholesterol more than 190 mg/dL.

We used self-reported race and categorized the patients as noted in JMH electronic health records, which included white Hispanic, white non-Hispanic, black Hispanic, black non-Hispanic, and unknown. Those who had missing race information were catalogued under unknown racial/ethnic classification.

Statistical analysis was conducted using SAS software, version 9.4. We performed descriptive analysis of sociodemographic characteristics, development of cerebrovascular risk factors, and differences in pharmacologic management of the established comorbidities based on patients' race. T-tests were performed for comparison of the means in development of the aforementioned risk factors and for comparing the differences between each race/ethnic group in the development of the previously mentioned comorbidities.

Results

Hundred eighty-eight women were identified for the study based on ICD-9 codes and 183 of these patients met inclusion criteria (Table 1). Five patients were excluded because they did not have a true preeclampsia diagnosis upon chart review or were deceased within the follow-up period. The average age of the study was 32.3 years of age (range 19-48). The mean duration of follow-up care was 2.9 years (range .1-4.7 years). Regarding insurance status, 55 patients (30.1%) had private health insurance, whereas 60 (32.8%) had federally funded insurance coverage, and 68 (37.1%) were uninsured/self-pay. The majority of the study population were black non-Hispanic (48%), followed by 35% white Hispanic, 8% black Hispanic, and 2% white non-Hispanic. Seven percent had unknown racial classifications. There was a significant difference in mean age among ethnic groups (P -value $< .01$). Mean average age was the oldest for white non-Hispanic (mean age = 34 years old) and the youngest for black Hispanic (mean age = 30.5 years old).

Compared to pre-pregnancy health status, the incidence of hypertension increased by 1.7 ($P < .05$), hyperlipidemia by 4.5 ($P < .05$), migraines by 2.2 ($P < .05$), and diabetes mellitus by 2 ($P < .05$) after a pregnancy with

Table 1. Patient characteristics

Total participants, N	188
Age, y (mean and SD)	32.3 (6.9)
Time elapsed between encounters, y	2.9
Race	(N, %)
Black non-Hispanic	88 (48)
White Hispanic	63 (35)
Black Hispanic	15 (8)
White non-Hispanic	4 (2)
Unknown	13 (7)

Table 2. Development of stroke risk factors

	Prepregnancy	Postpregnancy	P-value
Hypertension	35 (19.1%)	58 (31.7%)	<.05
Diabetes mellitus	9 (4.9%)	18 (9.8%)	<.05
Hyperlipidemia	2 (1.1%)	9 (4.9%)	<.05
Migraines	6 (3.3%)	13 (7.1%)	<.05

preeclampsia. Black non-Hispanics had higher rates of hypertension, obesity, and migraines (20.5%, 9.1%, and 6.8%, respectively) as compared to white Hispanics (15.9%, 6.3%, and 3.7%, respectively). There was no statistically significant association between insurance status (private versus federal or self-pay) and the development of one or more risk factor ($P = .072$; Table 2).

Regarding medical management of the developed cerebrovascular risk factor, 73.6% (42/57) of all hypertensive women were prescribed an antihypertensive medication, 88.9% (16/18) of women with diabetes were on pharmacologic therapy, yet no women with hyperlipidemia were prescribed a statin. Of the patients who developed hypertension, 74.3% of black non-Hispanics were prescribed an antihypertensive as compared to 55% of white Hispanics. For those with diabetes, 100% of black non-Hispanic subjects were pharmacologically managed compared to 77.8% of white Hispanics. There were no subjects in this study in either racial group that was on statin therapy for hyperlipidemia management. There was no statistically significant association between insurance status and the absence of medical management for one or more developed risk factors ($P = .68$).

Discussion

Our study found that, compared to their status before pregnancy, women with a history of preeclampsia have a statistically significant ($P < .05$) increased incidence of risk factors for stroke, specifically hypertension, hyperlipidemia, migraine headaches, and obesity. This supports prior studies that have suggested cerebrovascular disease and preeclampsia are expressions of the same disease process and that there be an adverse cardiovascular phenotype which predisposes mothers to hypertensive complications of pregnancy.^{7,8}

Among these women who developed such conditions after preeclampsia, only a fraction was being managed upon short-term follow-up within our health system. White Hispanic women, in particular, had lower rates of medical management regardless of insurance status. Our data suggests a need for the development of interventions to reduce the incidence of stroke in this population. While much research exists in determining the development of hypertension, hyperlipidemia, diabetes, and obesity after preeclampsia, there is not much research that helps establish a clear strategy of how to manage these risk factors. In fact, a minority of internists (9%) and obstetrician-

gynecologists (OB-GYNs) (38%) provide cardiovascular risk reduction counseling to women with a history of preeclampsia.⁴

This shortcoming is of concern, as there is great potential for early intervention and preventative medicine in the primary care setting. The young adult population is experiencing a rise in hospitalization rates for acute ischemic stroke and an increasing prevalence of stroke risk factors. Hypertensive disorders affecting up to 5%-10% of pregnancies, have been associated with the development of cardiovascular disease later in life.⁹ Thus, a history of preeclampsia allows providers an opportunity to identify patients who may be at an elevated lifetime risk for cardiovascular disease and provide interventions before disease has become established.

In response to a recent increase in female mortality rates, the American Heart Association and American College of Obstetricians and Gynecologists came together to publish a presidential advisory aimed at reducing cardiovascular disease among women.¹⁰ The emphasis of the advisory was promoting risk factor identification and early management through coordinated healthcare delivery alongside OB/GYNs. The advisory suggests that pregnancy be viewed as a natural "stress test," with adverse events such as preeclampsia being early warnings of increased risk of atherosclerotic cardiovascular disease. In fact, it is noted that preeclampsia is associated with a 2× increase in ischemic heart disease and stroke. This calls for the OB/GYN to identify these women as patients that need close follow up to monitor the development cardiovascular risk factors. Additionally, appropriate documentation of these risk factors in electronic medical records can facilitate improved transition of care to primary care physicians for medical management of risk factors and subsequent pregnancies.

This study is limited by the context in which patient follow up was determined. Each patient had different follow-up intervals and visits for different indications. There is a potential for lag time bias as the development of stroke risk factors increases with age. Additionally, potential for follow up in different health systems was not taken into account. There may also be selection bias, as only patients requiring follow-up encounters are included and many healthy subjects would not have had such encounters.

Summary

Our study found ethnic differences in the development of cerebrovascular risk factors during short-term follow up after preeclampsia. We also identified opportunities for quality improvement in reducing vascular risk factors. A systemic approach to management of vascular risk factors in women with a history of preeclampsia could reduce the burden of stroke among young and middle-aged women.

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