

EDITORIAL

# Are Strokes Declining Among Pregnant Women With Hypertensive Disorders of Pregnancy?

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**H**emorrhagic and ischemic strokes are a feared complication of pregnancy and a leading cause of maternal morbidity and mortality.<sup>1</sup> Of 100 000 pregnancies, 30 will be complicated by stroke, a 3-fold higher incidence than in nonpregnant women of reproductive age.<sup>2</sup> Pregnancy-associated strokes account for 10% of all strokes in women aged 12 to 44 years.<sup>3</sup> Given the growing number of ischemic strokes in young adults, and the subsequent disability and lifelong loss of productivity, characterization of the temporal trends of pregnancy-associated stroke is critical.

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**See Article by Wu et al.**

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Pregnancy-associated stroke can be associated with traditional vascular risk factors as well as pregnancy-specific conditions, including hypertensive disorders of pregnancy (HDP).<sup>1</sup> HDP include chronic hypertension, gestational hypertension, preeclampsia/eclampsia, and preeclampsia superimposed on chronic hypertension. Chronic hypertension predates pregnancy or is diagnosed at or before 20 weeks of gestation, whereas a new diagnosis after 20 weeks is called gestational hypertension. Preeclampsia is elevated blood pressure (systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg) during the same period as gestational hypertension, but with proteinuria or signs of end-organ dysfunction. HDP, particularly preeclampsia, are associated with

both hemorrhagic and ischemic strokes and cause a 4- to 5-fold increased risk of stroke.<sup>1,4</sup> Preeclampsia may also occur postpartum, and is a major contributor to postpartum stroke.<sup>5,6</sup> Data show that 36% of ischemic strokes and 58% of hemorrhage strokes in pregnancy and postpartum occur in women with preeclampsia.<sup>4</sup>

Studies have shown an increase in the frequency of stroke in women with HDP, with many events occurring in the postpartum period.<sup>7-9</sup> One of the largest nationwide studies showed a doubling in the rate of stroke in women with HDP from 1994 to 2011.<sup>10</sup> Most of these strokes occurred outside of the delivery hospitalization, with 42% of strokes diagnosed in the first 6 weeks postpartum.<sup>10</sup> It is unclear whether the temporal increase in stroke hospitalizations occurred during the antepartum, delivery, or postpartum period. A prior study demonstrated that pregnancy-associated strokes increased by 83% during postpartum hospitalizations but remained unchanged during delivery hospitalizations from 1994 to 1995 to 2006 to 2007.<sup>11</sup> The increased incidence of HDP conditions, such as preeclampsia, was thought to explain this increase in postpartum strokes.

The study by Wu and colleagues in this issue of the *Journal of the American Heart Association (JAHA)* explores the temporal trends, predictors, and outcomes of stroke in women with HDP during hospital admission for delivery.<sup>12</sup> The authors identified all HDP delivery hospitalizations in the nationally represented National Inpatient Sample between January 2004

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and December 2014 using validated *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes. They further extracted information on whether women with HDP had a stroke diagnosis during the delivery admission and classified these events as ischemic, hemorrhagic, or unspecified strokes based on *ICD-9-CM* codes. Ischemic strokes included cerebral venous thrombosis and transient ischemic attacks. Unspecified strokes included iatrogenic strokes and cerebrovascular complications of puerperium. Demographic information, vascular risk factors, obstetric information, acute stroke treatment, delivery complications, and cost outcomes were extracted from the data set for each patient. Temporal trend analysis was performed comparing the years 2004 to 2007, 2008 to 2011, and 2012 to 2014. Binary logistic regression analyses were used to determine the association of potential risk factors with stroke in women with HDP and the association between stroke and delivery complications of interest in fully adjusted models.

Among 4 240 284 HDP delivery hospitalizations, 3391 (0.08%) had a stroke event during admission. Most of these strokes (52.5%) occurred in women with preeclampsia. Among all hospitalizations for delivery, the proportion of deliveries in women with HDP increased from 8.4% to 10.9% over the study period. However, the proportion of deliveries in women with HDP and stroke decreased from 10 to 6 per 10 000 HDP delivery hospitalizations between 2004 and 2008 and remained stable until the end of the study period. The prevalence of cardiovascular diseases among women with HDP and stroke tripled during the study period. Compared with nonstroke cases, women with HDP and stroke were more likely to have vascular risk factors, including a history of stroke. Maternal mortality occurred in 8.8% of all stroke cases compared with 0.2% of nonstroke cases, corresponding to a 100-fold increase in the odds of mortality in women who experienced any stroke. Among the women with hemorrhagic stroke, 16% died during the admission, a 260-fold increase in the odds of mortality. Women with HDP and stroke were more likely to have delivery complications, such as cesarean section and postpartum hemorrhage, and other unfavorable outcomes, including longer hospital stays, higher hospital charges, and discharges to facilities.

This study advances our understanding of the relationship between HDP and pregnancy-associated stroke in several ways. First, the temporal increase in the proportion of HDP delivery hospitalizations highlights the importance of recognizing and treating women at high risk of developing preeclampsia.<sup>13,14</sup> The increase in the proportion of HDP deliveries may be attributable to several factors, including advanced maternal age and the associated risk factors, and a

trend toward fewer pregnancies among women in the United States.<sup>15,16</sup> Second, the results support the role of traditional vascular risk factors and coagulopathy in the risk of stroke in women with HDP, which may be attributable to women having children at an older age when vascular risk factors become more prevalent.<sup>1,10,17,18</sup> The third major finding relates to the maternal complications associated with stroke and HDP, including the 100-fold increase in the odds of maternal mortality. This finding further cements our understanding of stroke as a major cause of maternal mortality.

In contrast to prior studies, the authors found a decline in stroke among women with HDP. This conclusion may be related to the limitations of administrative claims data. Hemorrhagic and ischemic strokes remained largely unchanged, whereas unspecified stroke types declined over time. Such change could be attributable to improved accuracy of coding over time, leading to the improved classification of stroke-like symptoms. Transient ischemic attacks were included in the ischemic stroke category, but there is evidence for poor validity for the associated *ICD-9-CM* codes.<sup>19</sup> Our increased knowledge of pregnancy-associated stroke in the past 2 decades may have impacted the reported decline in strokes. Better awareness may have led to improved primary prevention and stroke reduction in women with HDP and lower pregnancy rates among women with a history of stroke. It is also possible that women with HDP earlier in the study period may have opted against any future pregnancies, which could have reduced the risk of stroke in later years. Finally, Wu and colleagues<sup>12</sup> examined stroke during delivery hospitalizations only. Recent trends in postpartum stroke among women with HDP remain unknown.

Stroke is a serious complication and a major cause of adverse outcomes in pregnancy and the postpartum period. Close monitoring and treatment of women at high risk for developing HDP during pregnancy, as well as management of vascular risk factors, may lower the risk of pregnancy-associated stroke. Wu and colleagues<sup>12</sup> showed that stroke in women with HDP may be declining during delivery hospitalizations. To truly understand whether strokes are declining, future studies should focus on recent trends and associated long-term outcomes of antepartum and postpartum stroke in women with HDP. Improving our knowledge of stroke in women with HDP during the antepartum, delivery, and postpartum period will help raise awareness of this complication and aid in counseling women on their stroke risk in current and future pregnancies. Our current understanding shows that clinicians should be attuned to recognize stroke symptoms in women with HDP to ensure prompt diagnosis and appropriate treatment aimed at preventing clinical deterioration.

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## ARTICLE INFORMATION

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### Disclosures

None.

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