The occurrence of a hypertensive pregnancy in a young woman gives sudden insight into the fragile nature of her vascular health, which has implications for the rest of her life. Women who have had a hypertensive pregnancy are more likely to present with hypertension within a few years of the pregnancy and have an increased risk of renal disease and heart disease over the subsequent decades. de Havenon et al report that women with hypertensive pregnancy also have an almost 4-fold higher risk of stroke within the 40 years after pregnancy, which the authors found to be associated with a history of preeclampsia, one of the more severe manifestations of hypertension in pregnancy.

To examine this association, de Havenon et al used publicly available data from participants in the Framingham Heart Study, for whom a lifetime of repeated prospective measurements of different risk factors are available. These detailed data extend over the 30 years between the episode of preeclampsia and subsequent cerebrovascular events, and the length of this span is important. The authors have developed a model that adjusts, year by year, for the consequences that varying exposures to vascular risk factors may have had for any underlying trajectory associating pregnancy with later disease. This model allows a much more precise estimate of the summary of exposure to different risk factors each woman received between the hypertensive pregnancy and the stroke. When this risk exposure is accounted for, the association between preeclampsia and later stroke becomes clear.

What may underlie this association? Hypertensive pregnancy is considered a systemic vascular disorder and thus has relevance to vascular beds throughout the body, including the brain. A hallmark of severe hypertensive pregnancy during preeclampsia is the changes that occur in cerebrovascular circulation, including edema and potential seizure. Recent data have indicated that changes in cerebrovascular structure and function are evident, even during young adulthood, in those with cardiovascular risk factors. Changes in white matter microstructure, which are characteristic of cerebrovascular damage, have also been found within 10 years of a hypertensive pregnancy. This damage is disproportionate to the extent of blood pressure elevation at the time of measurement. The presence of white matter lesions during midlife has been associated with a later risk of dementia and stroke, and the findings in women after a hypertensive pregnancy hint at an increasing trajectory toward cerebrovascular disease.

The findings and statistical approach of de Havenon et al also highlight something else. There may be opportunities to change the trajectory of disease. The association between preeclampsia and stroke only became apparent with adjustment for the subsequent lifetime exposure to risks. Therefore, it is likely that preventive behaviors and control of risk factors could be used to significantly modify the excess risk of cerebrovascular disease among those who develop preeclampsia. However, at this stage, the findings are essentially based on computational predictive models built from Framingham Heart Study data, and further work is needed to extract clinical meaning.

The Framingham Heart Study cohort represents individuals with homogeneous ethnicity from a single geographic area, and we do not know whether the results can be generalized. The definition of hypertensive disorder lacked detail, as it was based on self-reporting of toxemia (the terminology used in 1948, when the Framingham Heart Study began) and therefore is not consistent with current definitions of hypertensive pregnancy. Whether risk is significantly higher among some women or is associated with certain types of hypertensive disorder requires clarification. The most important
type of work needed to translate these observations into clinical use is the performance of clinical trials. This research would allow tests to be conducted to determine whether interventions provided at different stages of life or around the time of pregnancy could modify the disease progression associated with preeclampsia. To support these clinical trials, effective tools to capture information on current disease states in the heart, brain, or other organs are required to examine the ways in which interventions can modify the preclinical stages of disease.

Nevertheless, the associations between hypertensive pregnancy and later vascular diseases, such as stroke, are clear. The onus is now on identifying ways to take advantage of this information and prevent future harmful vascular events.

REFERENCES


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