Hypertension disorders of pregnancy increase risk of premature maternal mortality

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Women who experienced hypertensive disorders of pregnancy (HDPs) but did not develop chronic hypertension have a greater risk of premature mortality, specifically cardiovascular disease (CVD)-related deaths, according to a study published in the *Journal of the American College of Cardiology* (*JACC*). A separate *JACC* study examined the cardiovascular health risks associated with pregnancy in obese women with heart disease.

HDPs, which occur in approximately 10% of all pregnancies worldwide, are among the most common health issues during pregnancy. There are four types of HDPs: chronic hypertension, gestational hypertension (GHTN), preeclampsia and chronic hypertension with superimposed preeclampsia. GHTN and preeclampsia, which occur at or after 20 weeks' gestation, are leading causes of maternal and perinatal morbidity and mortality. While women with a history of HDPs have a three to five times higher risk of developing chronic hypertension, it is unclear whether the association between HDPs and premature mortality (death before age 70) can be attributed to women developing chronic hypertension. The authors of this study sought to examine the links between GHTN and preeclampsia, the subsequent development of hypertension, and all-cause and cause-specific premature mortality.

Researchers of this paper looked at 88,395 ever pregnant female nurses 25-42 years old who participated in the Nurses' Health Study II, focusing on GHTN and preeclampsia within the term HDPs. Using questionnaires from 1989-2017, the nurses' health study collected information on reproductive characteristics and lifestyle and health-related conditions over three decades. To determine whether the association between HDPs and premature mortality was explained by the subsequent development of chronic hypertension and whether this link exists among women who didn't develop chronic hypertension, the authors classified women as the following: No HDPs and chronic hypertension, HDPs only, chronic hypertension only or both HDPs and subsequent chronic hypertension.

Results of the study showed 12,405 women, or 14%, experienced HDPs in at least one of their pregnancies. Compared to women without HDPs, women who experienced GHTN and/or preeclampsia had a greater baseline BMI, gestational diabetes, parental history of diabetes and MI/stroke and chronic hypertension. During 28 years of follow-up, there were 2,387 premature deaths, including 212 CVD deaths. A history of GHTN or preeclampsia was associated with a 42% increase in premature mortality. This association remained significant after adjusting for confounders as well as for post-pregnancy dietary, lifestyle and reproductive characteristics over time. Women with

a history of HDP had over a twofold higher risk of premature CVD mortality. When authors examined the subsequent development of chronic hypertension, they found an elevated risk of all-cause premature CVD mortality in women with HDPs only, chronic hypertension only and both HDPs and subsequent chronic hypertension.

"Our results suggest that HDPs, either GHTN or preeclampsia, was associated with a greater risk of premature mortality, especially CVD-related deaths, even in the absence of chronic hypertension," said Jorge E. Chavarro, MD, ScD, associate professor of nutrition and epidemiology at the Harvard T.H. Chan School of Public Health and of medicine at Brigham and Women's Hospital and Harvard Medical School in Boston, and corresponding author of the study. "Our results highlight the need for clinicians to screen for the history of HDPs when evaluating CVD morbidity and mortality risk of their patients."

There are some limitations of this study, including the diagnosis of HDPs and chronic hypertension were self-reported, which can result in misclassification of disease status and biased risk estimates, and the study's population mainly consisted of non-Hispanic white women, so its findings may not be generalized to ethnic and racial minority groups. However, authors of an accompanying editorial comment praise the significance of the study's findings.

"The authors should be applauded on raising a biologic plausibility of HDP's independent association with premature all-cause mortality," said Garima Sharma, MD, assistant professor of medicine in the division of cardiology and department of medicine at the Johns Hopkins University School of Medicine, and corresponding author of the editorial comment. "Contemporary management of women with HDPs will need better risk assessment tools informed by precision medicine to appropriately identify those women who are at greatest risk of premature CVD and to develop algorithms for early intervention in order to change the trajectory of these women."

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While this paper adds to the growing evidence that health conditions pregnant women experience can influence their health later in life, the effect of already having heart disease while pregnant is also a huge health concern. Another study in *JACC* focused on the impact of maternal obesity on pregnancy complications in women with heart disease. Authors of that paper found women with heart disease and obesity had higher rates of cardiac complications during pregnancy compared to women with normal weight.

"Pregnant women with heart disease and obesity should be educated about these risks, and health care providers should ensure that dietary advice, weight gain recommendations, and that obesity and other comorbidities are addressed as part of routine care," said Candice Silversides, MD, cardiologist at Mount Sinai and Toronto General Hospital in Toronto, and corresponding author of the study. "Postpartum surveillance is important in pregnant women with obesity because of the increased risk of complications during this time period."

More information: Jorge E. Chavarro et al, Hypertensive Disorders of Pregnancy and Subsequent Risk of Premature Mortality, *J Am Coll Cardiol.* DOI: 10.1016/j.jacc.2021.01.018
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