Migraine associated with increased risk for pregnancy complications

January 31 2023

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Women are disproportionately affected by migraine, especially during their reproductive years. However, the relationship between migraine and adverse pregnancy outcomes has not been well understood. A new

study by investigators from Brigham and Women's Hospital, a founding member of the Mass General Brigham healthcare system, analyzed data from thousands of women from the Nurses' Health Study II to assess the relationship between migraine and pregnancy complications.

In a paper published in *Neurology*, the team reports that migraine diagnosed prior to pregnancy was linked to adverse outcomes during pregnancy, including preterm delivery, gestational hypertension, and preeclampsia, suggesting that migraine may be a clinical marker of elevated obstetric risk.

"Preterm delivery and hypertensive disorders are some of the primary drivers of maternal and infant morbidity and mortality," said first author Alexandra Purdue-Smithe, Ph.D., associate epidemiologist at Brigham and Women's Hospital and instructor in Medicine at Harvard Medical School. "Our findings suggest that a history of migraine warrants consideration as an important risk factor for these complications and could be useful in flagging women who may benefit from enhanced monitoring during pregnancy."

Women are two to three times more likely than men to experience migraine in their lifetime, and migraine is most prevalent among women between the ages of 18 and 44. For some, the migraine headaches can be accompanied by aura (5.5% of the population), which are usually visual disturbances that appear prior to headache onset.

Adverse pregnancy outcomes and migraine, especially migraine with aura, are each consistently associated with higher risk of coronary heart disease and ischemic stroke in women according to prior studies. The underlying biology responsible for these risks might also increase the likelihood of pregnancy complications. But to date, only a few small or retrospective studies have examined migraine as a risk factor for pregnancy complications. No prospective studies have examined risks by

aura phenotype (migraine with versus without aura).

Purdue-Smithe and colleagues analyzed data from the large, prospective Nurses' Health Study II, which included 30,555 pregnancies from 19,694 U.S. nurses. Investigators looked at pre-pregnancy self-reported physician-diagnosed migraine and migraine phenotype (migraine with and without aura) and incidence of self-reported pregnancy outcomes.

Due to the large size of the study population and availability of data on other health and behavioral factors, researchers could control for potential confounding factors in their analyses, such as body mass index, chronic hypertension, and smoking.

Researchers found that pre-pregnancy migraine was associated with a 17 percent higher risk of preterm delivery, 28 percent higher rate of gestational hypertension, and 40 percent higher rate of preeclampsia compared to no migraine. Migraine with aura was associated with a somewhat higher risk of preeclampsia than migraine without aura. Migraine was not associated with low birth weight or gestational diabetes mellitus.

Participants with migraine who reported regular aspirin use (more than twice weekly) prior to pregnancy had a 45 percent lower risk for preterm delivery. The US Preventive Services Task Force currently recommends low-dose aspirin during pregnancy for individuals at high risk of preeclampsia and those who have more than one moderate risk factor for preeclampsia. Clinical trials have shown that low-dose aspirin during pregnancy is also effective at reducing rates of preterm birth.

However, Purdue-Smithe notes that migraine is currently not included among indications for aspirin use in pregnancy. "Our findings of reduced risk of preterm delivery among women with migraine who reported regular aspirin use prior to pregnancy suggests that aspirin may also be

beneficial for women with migraine. Given the observational nature of our study, and the lack of detailed information on aspirin dosage available in the cohort, clinical trials will be needed to definitively answer this question."

Some other limitations of the study include that, participants only reported if they had a physician-diagnosis of migraine, likely excluding those who did not have chronic or severe migraine. Further, aura was assessed after the migraine diagnosis and after many of the pregnancies in the cohort, possibly resulting in some degree of reverse causation in analyses examining migraine phenotype. Additionally, the cohort study consists of predominantly non-Hispanic white individuals with relatively high socioeconomic status and health literacy, which could limit generalizability.

More information: Alexandra C Purdue-Smithe et al, Prepregnancy Migraine, Migraine Phenotype, and Risk of Adverse Pregnancy Outcomes, *Neurology* (2023). DOI: 10.1212/WNL.0000000000206831

Provided by Brigham and Women's Hospital