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Migraine and adverse pregnancy outcomes: the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be

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Keywords

migraine; headache; hypertensive disorders of pregnancy; preeclampsia; preterm birth; adverse pregnancy outcomes

Objective:

Migraine affects 28% of women in their pregnancy-capable years,[1] and is associated with systemic inflammation, endothelial dysfunction, and increased risk of pregnancy-associated thromboembolic events.[2, 3] Migraine history has been associated with adverse pregnancy outcomes (APO) of placental origin, including hypertensive disorders of pregnancy (HDP) and preterm birth (PTB).[4] We tested the hypothesis that self-reported migraine in nulliparous individuals is associated with higher odds of APO.

Study Design:

The multi-center Nulliparous Pregnancy Outcomes Study Monitoring Mothers-to-be (nuMoM2b) study enrolled 10,038 nulliparous US participants with singleton gestation in early pregnancy, following them prospectively through delivery.[5] Medical histories were collected from study participants by standardized interview: participants were asked “Have

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you ever had any of the following medical conditions or diagnoses?" followed by a list of diagnoses, which included "migraine headaches." We considered participants who responded "yes" to this question at the first-trimester study visit to have a migraine history. We defined "APO" as ≥1 of the following outcomes, defined according to standardized definitions and adjudicated by maternal-fetal medicine specialists after delivery: gestational hypertension, preeclampsia/eclampsia, PTB (medically indicated or spontaneous), small-for-gestational-age at birth, or stillbirth. We compared characteristics between participants who did and did not report migraine, including demographics, family history of preeclampsia, and comorbidities such as obesity, recent smoking, chronic hypertension, chronic kidney disease, pre-gestational diabetes and autoimmune disorders. We created logistic regression models to estimate odds ratios (OR) and 95% confidence intervals (95% CI) for the association of migraine with APO, adjusting for characteristics that showed between-group differences ($p<0.1$) in univariable analysis. In secondary analyses, we estimated associations between migraine and individual APOs, and tested for interactions between migraine and chronic hypertension, obesity, and diabetes. We performed sensitivity analyses restricting the exposed group to 1) those who reported using migraine medications within the last two months, and 2) those who reported migraine headaches at all four study visits during the pregnancy.

Results:

Of 9,450 participants with complete data included in the analysis, 1,752 (19.1%) reported a diagnosis of migraine at visit 1. Cohort characteristics are presented in the Supplement. Age, income level and body mass index did not differ between exposure groups. Participants with migraine had higher proportions of self-identified white race, recent smoking history, autoimmune disorders, and chronic kidney disease. Adjusting for all factors which differed to $p<0.1$ in univariable analysis, participants with migraine had increased odds of any APO (adjusted OR 1.26, 95% CI 1.12, 1.41). For individual APO, participants with migraine had higher odds of any HDP, and both medically indicated and spontaneous PTB, but not small-for-gestational age or stillbirth (Table). There were no significant interactions between migraine and obesity, chronic hypertension or diabetes. Sensitivity analyses showed a larger effect in participants who reported recent medication use (adjusted OR 1.49, 95% CI 1.18, 1.88).

Conclusion:

In a diverse, prospective cohort of 9,450 nulliparous US participants, self-reported migraine headaches were associated with 26% higher odds of APO, an effect driven by HDP and both medically-indicated and spontaneous PTB. Migraine may be an underrecognized risk factor for APO.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table.

Adverse pregnancy outcomes in nuMoM2b participants, with and without migraine

	Migraine (N=1752)	**No Migraine (N=7698)**	**Unadjusted OR* (95% CI)**	**Adjusted OR* (95% CI)**
	N (%)	**N (%)**		
Any APO	700 (40.0)	2658 (34.5)	**1.26 (1.13–1.40)**	**1.26 (1.12–1.41)**
Any hypertensive disorder of pregnancy	451 (25.7)	1738 (22.6)	**1.19 (1.06–1.34)**	**1.18 (1.04–1.33)**
- Gestational Hypertension	273 (15.6)	1082 (14.1)	1.13 (0.98–1.30)	1.12 (0.96–1.30)[1]
- Preeclampsia or eclampsia (including superimposed preeclampsia)	178 (10.2)	656 (8.5)	**1.22 (1.02–1.44)**	1.18 (0.97–1.41)
Stillbirth	12 (0.7)	45 (0.6)	1.17 (0.59–2.15)	0.97 (0.42–1.99)
Preterm Birth	186 (10.6)	599 (7.8)	**1.41 (1.18–1.67)**	**1.44 (1.19–1.73)**
- Medically indicated	77 (4.4)	232 (3.0)	**1.48 (1.13–1.92)**	**1.44 (1.08–1.89)**
- Spontaneous	109 (6.2)	367 (4.8)	**1.33 (1.06–1.65)**	**1.40 (1.11–1.77)**
Small for Gestational Age	206 (11.8)	811 (10.5)	1.13 (0.96–1.33)	1.16 (0.97–1.38)
Sensitivity Analysis 1	*Migraine with medication use, visit 1 (N=332)*	*No Migraine (N=7698)*	*Unadjusted OR*(95% CI)*	*Adjusted OR*(95% CI)*
	N (%)	*N (%)*		
Any APO	*146 (44.0)*	*2658 (34.5)*	***1.49 (1.19–1.86)***	***1.49 (1.18–1.88)***
Sensitivity Analysis 2	*Reported migraine all 4 visits (N=1011)*	*No Migraine (N=7698)*	*Unadjusted OR*(95% CI)*	*Adjusted OR*(95% CI)*
	N (%)	*N (%)*		
Any APO	*413 (40.9)*	*2658 (34.5)*	***1.31 (1.14–1.50)***	***1.32 (1.15–1.52)***

OR: odds ratio. CI: confidence interval. APO: adverse pregnancy outcome. Models were adjusted for the following covariates which differed significantly between exposure groups (p<0.1) in univariable analysis: race/ethnicity, chronic hypertension, renal disease, autoimmune disorders (systemic lupus erythematosus or antiphospholipid syndrome), smoking in the 3 months prior to pregnancy, and family history of preeclampsia in mother or sister.

*Bolded ORs indicate p<0.05.

[1]Chronic hypertension not included in adjusted model for outcome of gestational hypertension.

Sensitivity Analysis 1: Exposure group defined as those who reported migraine headaches with medication use within the last two months at visit 1

Sensitivity Analysis 2: Exposure group defined as those who reported migraine headaches at all four study visits