

## Preexisting cerebrovascular disease in pregnancy: a case series of neurologic and obstetrical outcomes

**OBJECTIVE:** Uncertainty remains regarding neurological and obstetrical risks during pregnancy for patients with preexisting cerebrovascular disease (pCVD).

**STUDY DESIGN:** We reviewed medical records of 35 patients with pCVD evaluated in a neuro-obstetrics clinic embedded within a maternal-fetal medicine practice at an urban academic medical center between August 2019 and December 2021. The patients were referred for neurological evaluation during or before pregnancy. We describe maternal and fetal adverse pregnancy outcomes (APO) as well as delivery mode, postpartum readmissions (within 6 weeks of delivery), and acute cerebrovascular events (within 6 weeks of delivery) (Supplement). We compared characteristics between patients with and without APO using chi-square and parametric or nonparametric tests as appropriate (alpha<.05). Statistical analyses were performed using Stata-v.16 (StataCorp LLC, College Station, TX). Columbia University's Institutional Review Board granted approval.

**RESULTS:** We included 35 patients with pCVD with 36 pregnancies: 17 with transient ischemic attack (TIA) or arterial ischemic stroke (AIS), 2 with hemorrhagic stroke, 5 with venous sinus thrombosis (VST), 5 with unruptured cerebrovascular lesions, and 6 with other or multiple disorders. Baseline characteristics of patients with and without APO are shown in the Table. Most patients (80%) had at least 1 stroke risk factor, with structural heart conditions (31%) as the most common. All patients with previous TIA, AIS, or VST received antithrombotics (Supplement).

APO occurred in 51% of patients and included preterm birth (PTB; 29%), small for gestational age (20%), and hypertensive disorders of pregnancy (HDP; 20%). Baseline characteristics did not differ significantly in those who developed APO compared with those who did not. All PTBs were medically indicated for nonneurologic reasons. No patients were recommended for primary cesarean delivery based on neurologic diagnosis. Avoidance

of prolonged second stage of labor was advised for previous dissections, unruptured cerebral aneurysms, and intracerebral hemorrhage. Cesarean deliveries occurred for 43% of patients, all for obstetrical indications. Two patients were readmitted: 1 for headache with normal imaging, and 1 for an obstetrical complication. One patient had recurrent postpartum reversible cerebral vasoconstriction syndrome (RCVS) with no readmission. Pregnancy outcomes by pCVD are shown in the Supplementary Materials. **CONCLUSION:** Patients with pCVD may present to maternal-

fetal medicine specialists for preconception and prenatal counseling. Limited data, particularly for nonstroke patients with pCVD, make counseling challenging, and some patients report abstaining from pregnancies or undergoing primary cesarean deliveries.<sup>1–4</sup>

In our study, acute cerebrovascular event recurrence during pregnancy and postpartum was rare, occurring in 1 of 35 patients. Our results align with studies showing low rates of recurrent stroke, VST, cervical artery dissection, and RCVS.<sup>1–3,5</sup> However, rates of certain APO, particularly HDP, were high compared with the general population (Supplement). It is possible underlying comorbidities, lifestyle factors, or genetic predisposition, may contribute to pathophysiological mechanisms that increase the risk of both cerebrovascular diseases and APO. Study limitations include pCVD etiology heterogeneity, small sample size, 6-week follow-up time-frame, and selection bias.

However, to the best of our knowledge, this is the first study to report detailed maternal and fetal obstetrical outcomes in pregnant patients with pCVD. Future, prospective studies should assess the role of shared underlying pathophysiological mechanisms in cerebrovascular disease and pregnancy outcomes in this population.

**SUPPLEMENTARY MATERIALS:** Supplementary material associated with this article can be found in the online version at doi:10.1016/j.xagr.2023.100233.

| TABLE   Baseline characteristics by whether or not patients experienced adverse pregnancy outcomes |            |                       |             |         |
|--|------------|-----------------------|-------------|---------|
| Characteristic   | Total n=35 | APO <sup>a</sup> n=18 | No APO n=17 | P value |
| Preexisting CVD  |            |                       |             | .61     |
| TIA/ arterial ischemic stroke  | 17 (49%)   | 9 (50%)               | 8 (47%)     |         |
| Hemorrhagic stroke <sup>b</sup>  | 2 (6%)     | 1 (6%)                | 1 (6%)      |         |
| Venous sinus thrombosis  | 5 (14%)    | 1 (6%)                | 4 (24%)     |         |
| Unruptured vascular lesion   | 5 (14%)    | 3 (17%)               | 2 (12%)     |         |
| Other <sup>c</sup>   | 6 (17%)    | 4 (22%)               | 2 (12%)     |         |
| Race or ethnicity  |            |                       |             | .87     |
| Non-Hispanic White   | 17 (49%)   | 9 (50%)               | 8 (47%)     |         |
| Non-Hispanic Black   | 3 (9%)     | 1 (6%)                | 2 (12%)     |         |
| Hispanic or Latinx   | 12 (34%)   | 6 (33%)               | 6 (35%)     |         |
| Other or unknown   | 3 (9%)     | 2 (11%)               | 1 (6%)      |         |
| Maternal age at delivery in years  | 33 (20-46) | 33 (20-46)            | 30 (26-34)  | .66     |
| Nulliparous  | 22 (63%)   | 13 (72%)              | 9 (53%)     | .24     |
| Male fetal sex   | 15 (43%)   | 8 (44%)               | 7 (41%)     | .85     |
| Initial cerebrovascular diagnosis during pregnancy   | 12 (34%)   | 5 (28%)               | 7 (41%)     | .40     |
| During index pregnancy   | 6 (17%)    | 4 (22%)               | 2 (12%)     | .41     |
| During previous pregnancy  | 6 (17%)    | 1 (6%)                | 5 (29%)     | .06     |
| Antithrombotics used during index pregnancy or the postpartum                                      | 29 (83%)   | 14 (78%)              | 15 (88%)    | .41     |
| At least 1 stroke risk factor <sup>d</sup>   | 28 (80%)   | 15 (83%)              | 13 (76%)    | .61     |
| Chronic hypertension   | 7 (20%)    | 3 (17%)               | 4 (24%)     | .61     |
| Diabetes mellitus  | 4 (11%)    | 2 (11%)               | 2 (12%)     | .95     |
| Hyperlipidemia   | 1 (3%)     | 1 (6%)                | 0 (0%)      | .32     |
| Obesity  | 8 (23%)    | 3 (17%)               | 5 (29%)     | .37     |
| Smoking  | 1 (3%)     | 1 (6%)                | 0 (0%)      | .32     |
| Structural heart disease   | 11 (31%)   | 6 (33%)               | 5 (29%)     | .80     |
| Abnormal heart rhythm  | 3 (9%)     | 1 (6%)                | 2 (12%)     | .51     |
| Connective tissue disorder   | 2 (6%)     | 1 (6%)                | 1 (6%)      | .97     |
| Genetic hypercoagulable state  | 8 (23%)    | 4 (22%)               | 4 (24%)     | .93     |
| Acquired hypercoagulable state   | 6 (17%)    | 4 (22%)               | 2 (12%)     | .41     |
| Migraine   | 20 (57%)   | 11 (61%)              | 9 (53%)     | .63     |
| Advanced maternal age <sup>e</sup>   | 10 (29%)   | 6 (33%)               | 4 (24%)     | .52     |
| In vitro fertilization pregnancy   | 4 (11%)    | 3 (17%)               | 1 (6%)      | .32     |
| History of APO in previous pregnancy <sup>a</sup>  | 9 (26%)    | 3 (17%)               | 6 (35%)     | .21     |

Data are shown as numbers (percentage) or medians (total range).

APO, adverse pregnancy outcomes.

<sup>a</sup> APO defined as: hypertensive disorders of pregnancy (excluding chronic hypertension), gestational diabetes mellitus, placental abruption, first trimester pregnancy loss, intrauterine fetal demise, fetal growth restriction, small for gestational age infant, and preterm birth (medically indicated or spontaneous); <sup>b</sup> Hemorrhagic strokes included 1 subarachnoid hemorrhage and 1 intracerebral hemorrhage; <sup>c</sup> Other cases included 2 reversible cerebral vasoconstriction syndrome, 1 cervical artery dissection, 1 cervical artery dissection with TIA, 1 Moyamoya disease with ischemic stroke, and 1 Moyamoya disease with ischemic stroke and unruptured aneurysm; <sup>d</sup> Underlying stroke risk factors included: chronic hypertension, diabetes mellitus, hyperlipidemia, obesity, smoking, structural heart condition (including patent foramen ovale, congenital heart disease (eg, atrial septum defect, ventricular septal defect, double outlet left ventricle, transposition of the great vessels), abnormal heart rhythms (eg, bradycardia, atrial flutter or fibrillation, supraventricular tachycardia), hypercoagulable state from genetic factors (eg, Factor V Leiden, sickle cell trait, sickle cell disease), acquired hypercoagulable state (eg, antiphospholipid syndrome, cancer, chronic autoimmune diseases) and connective tissue disorders (eg, fibromuscular dysplasia, systemic lupus erythematosus); <sup>e</sup> Advanced maternal age defined as age >35 years at time of delivery.

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