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### Corresponding Author

S. Madhumita,  
Department of Emergency  
Medicine, Apollo Hospitals, Chennai,  
Tamil Nadu, India

### Author Designation

<sup>1,3</sup>Junior Consultant

<sup>2</sup>Head and Clinical

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## A Review of the Literature on Acute Ischemic Stroke During Pregnancy: Case Report

<sup>1</sup>S. Madhumita, <sup>2</sup>A. Dhavapalani and <sup>3</sup>Srinivasan Dhanasekaran

<sup>1-3</sup>Department of Emergency Medicine, Apollo Hospitals, Chennai, Tamil Nadu, India

### Abstract

Pregnancy and puerperium are major risk factors for stroke in young women, which is a cause of significant mortality (7.7-15%)<sup>[1]</sup> and morbidity. Around 50% of women are left with neurological impairment [1] which leads to persistent disability. Pregnancy by itself is a risk factor for thrombotic events due to various physiological and pathological alterations. The lack of guidelines and RCTs leads to lack of insight on various treatment options. Hence future prospective studies are required to fill in knowledge gaps to guide appropriate treatment strategies and for aggressive risk factor modification strategies. Here we present 2 pregnant women in third trimester who came with acute ischemic stroke to a tertiary care ED in India, who were thrombolysed and had successful neurological outcomes and no obstetric complications.

## INTRODUCTION

**Case 1:** 31 Year old, G<sub>4</sub> P<sub>1</sub> L<sub>1</sub> A<sub>2</sub>, 30 weeks pregnant women came with giddiness, vomiting and left sided weakness since 1 hour. She had history of pregnancy induced hypertension, on prophylactic Aspirin.

**On Arrival:** Vitals were stable, ABC no issues. Her GCS was 15/15. She had complete paralysis on the left upper limb and lower limb with left sided upper motor neuron facial palsy. NIHSS was 11. Her CBG, electrolytes and ECG were normal. MRI was done which showed acute infarction in right posterior cerebral artery territory. Multiple consults were sought and with informed consent and ruling out contraindications for Thrombolysis she received Alteplase IV 0.9mg/kg. She was shifted to ICU for further care. After her clinical condition improved, she was discharged on day 7 with Modified Rankin score of 1. She delivered a healthy baby at 40 weeks.

**Case 2:** 31 years primigravida at 33 weeks of gestation, presented with acute onset weakness in the left upper limb and lower limb since 2 hours, accompanied by headache since last night.

On arrival, vitals were stable. ABC no issues. GCS was 15/15. Neurologic examination revealed 3/5 power on the right upper limb and lower limb with right side upper motor neuron facial palsy with NIHSS score of 8. CBG, electrolytes and ECG were normal. MRI brain showed acute infarct in right thalamus, right hippocampus and right occipital lobe and attenuated right PCA distal to its P2 segment. Multiple consults sought and with informed consent and ruling out contraindications for thrombolysis, she received Alteplase IV 0.9mg/kg. She was shifted to ICU for further care. All work up for prothrombotic state were negative. Her clinical condition improved and she was sent home on day 6 with Modified Rankin score of 2. At 38 weeks, she delivered a healthy baby.

## RESULT AND DISCUSSION

One of the main causes of maternal death and morbidity during pregnancy is stroke and is now becoming a global concern<sup>[1]</sup>. 30-50% of stroke survivors have long term neurological disability<sup>[2]</sup>. Stroke in pregnancy is thought to be multi factorial, among which pregnancy by itself is a major stroke risk factor. The various physiological changes in keeping with Virchow's triad of increased prothrombotic factors along with decreased anti thrombotic factors, venous stasis and endothelial and vessel wall changes contribute to increased risk of thrombotic events.

Pregnant women with hypertensive disorders have a five-fold increased risk of stroke and it is a preventable risk factor if identified and treated early<sup>[2]</sup>. Data shows that increasing maternal age increases the odds of incidence of stroke.

A prospective study done in India in 2006-2008 reported the rate of preeclampsia/eclampsia is around 73% common among women who had pregnancy-related stroke<sup>[3]</sup>.

Compared to 89 per 100,000 deliveries in low-and middle-income nations, the incidence of maternal stroke in high-income countries was 30 per 100,000 pregnancies according to a pooled data from 11 studies that included more than 85 million pregnant and postpartum women<sup>[4]</sup>.

Review of published data (Ovid Medline, EMBASE, and ISI Web) over a period of 27 years showed that the incidence of ischemic and hemorrhagic stroke were almost similar<sup>[5]</sup>.

There is scarcity of data regarding Thrombolysis in pregnancy from India, especially in the last trimester of pregnancy, with only 3 case reports in total published so far<sup>[6]</sup>.

However, the highest incidence of maternal stroke is noted in the third trimester and in the first 6 weeks postpartum<sup>[7]</sup>.

A thorough history and examination are needed to rule out stroke mimics<sup>[8]</sup>.

The initial imaging modality of choice is CT brain due to its widespread availability and shorter duration<sup>[8]</sup>. The risk of radiation related effects on single CT exposure is way below the safety threshold for teratogenicity<sup>[9]</sup>.

MRI is safe in all trimesters<sup>[10]</sup> but Gadolinium contrast is listed as FDA class C drug hence should be avoided. MRI is better than CT as it helps in early identification of infarcts and other lesions<sup>[10]</sup>.

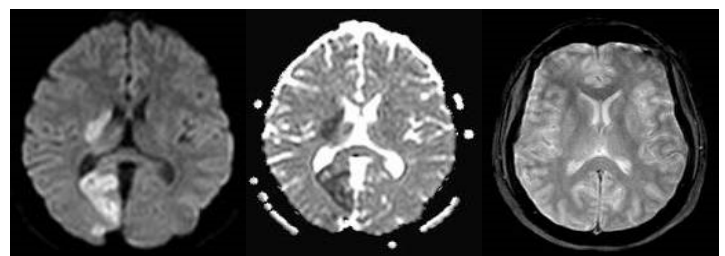


Fig. 1: MRI DWI MRI ADC MRI Flair



Fig. 2: MRI DWI MRA MRA-day 2 Revascularised

Blood work up include tests for identifying hypercoagulable states and other basic investigations. Blood work up should not delay imaging or treatment decisions in acute CVA<sup>[11]</sup>. Echocardiography should be obtained to look for cardiac source of emboli in suspected embolic strokes<sup>[12]</sup>.

Treatment at a primary stroke centre will facilitate both thrombolytic therapy and or bridging endovascular therapy<sup>[13]</sup>.

Acute stroke management in pregnant women should be done by multidisciplinary approach with consults from obstetrics and gynaecology, neurology, neonatology and interventional radiology if available<sup>[14]</sup>.

Thrombolytic therapy is indicated if benefits outweigh the risk and no other contraindications for thrombolysis are present. No RCTs are available at present but data from observations suggest thrombolytic therapy is safe and effective<sup>[15]</sup>.

AHA recommends IV thrombolysis in pregnancy and has removed it from the list of contraindications<sup>[16]</sup>. The risk associated with IV TPA seems low in pregnancy compared with the debility of long-standing neurological deficits. The decision on thrombolysis depends on patient factors, clinical and radiological findings like DWI/perfusion mismatch and large vessel occlusion with obstetric backup<sup>[17]</sup>.

In an analysis of 338 pregnant and postpartum women from American Heart Association's Get With the Guidelines-Stroke Registry from 2008-2013 treated with reperfusion therapy, the short-term outcomes between pregnant and postpartum women in comparison with nonpregnant women were similar despite increased severity of maternal strokes.

According to 2019 American Heart Association/American Stroke Association guidelines, IV alteplase can be used if benefits outweigh the risk<sup>[8,18]</sup>. Due to large molecular weight of alteplase, it does not cross the placenta. Therefore, alteplase is not known to pose direct intracranial or systemic bleeding risks to the fetus<sup>[10]</sup>. Studies on animal embryos have not demonstrated any teratogenic effects of IV TPA<sup>[17]</sup>.

Dose of IV alteplase is 0.9 mg/kg (maximum of 90 mg) calculated according to prepregnancy or early pregnancy weight<sup>[19]</sup>.

No RCTs are available on comparison of efficacy and adverse effects among different thrombolytics agents in pregnancy Thrombolysis.

Literature review of 141 pregnant women from database MEDLINE on thrombolysis in pregnancy, only 2.8% had maternal deaths and 8.2% had major bleeding episode and they have concluded that the risks are not greater than general population receiving thrombolytic therapy<sup>[15]</sup>.

Both mechanical thrombectomy and IVT should be considered in patients with large vessel occlusion<sup>[13]</sup>. The estimated recurrence risk in future pregnancy was 1 percent at one year and 2.3 percent at five years<sup>[14]</sup>.

Maternal stroke is not a contraindication for normal delivery. Women who have increased risk of ICH should be taken up for caesarean section<sup>[2]</sup>.

Tools for risk stratification are currently unavailable. High risk pregnant women should be identified and focus should be on aggressive risk factor treatment, risk factor prevention and counselling and community preventative measures, especially in high-risk populations.

Both our patients presented in third trimester of pregnancy. First patient had associated hypertensive disorder of pregnancy. MRI brain revealed acute infarcts in both the patients. As both the patients presented in window period and had no contraindications for thrombolysis, as benefits outweigh the risk, they were thrombolysed successfully with IV alteplase as per the above recommendations. Both the patients had uneventful hospital stay and were discharged. Both of them delivered healthy babies at term.

## CONCLUSION

Pregnancy is a major risk factor for stroke. No RCT or guidelines are available till date to guide management in these patients. Multiple systemic reviews and case reports suggest thrombolysis in pregnancy is safe if no contraindications exist. Thrombolytic agent of choice is alteplase as per AHA recommendation and no major adverse effects are found on the fetus.

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