

## Cerebrovascular Complications in Pregnancy and Puerperium

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### Abstract

**Objectives** The aim of this study was to analyze the incidence, possible etiological factors, pathology, clinical manifestations, brain CT scan features, treatment, and prognosis of cerebrovascular complications occurring in pregnancy and puerperium.

**Methodology** This is a prospective analytical study conducted at the Govt. Hospital for women and children, Chennai, from January 2006 to February 2008. During the above period, 26 women were diagnosed with various cerebrovascular complications. In these patients, the clinical data, risk factors, neurological features, investigations, results, and neuroimaging reports were analyzed.

**Results** The incidence of cerebrovascular complications in this study was 66 per 100,000 deliveries. None had prior history of diabetes, hypertension, renal disease, or seizure disorder. Two women were suffering from cardiac disease. PET and eclampsia were seen in 19/26 (73 %) cases. Seven women were suffering from anemia and one with severe sepsis. The neurological complications manifested predominantly in the postpartum period. Cases presented with

hemiplegia/ facial palsy and aphasia. CT scan imaging showed intracerebral hemorrhage in four cases, cerebral infarcts in five cases, and cortical vein thrombosis in 16 cases. There were five maternal deaths in this study.

**Conclusion** Stroke occurring in pregnancy, though rare, is a serious complication which can lead to maternal death. In this study, hypertension has emerged as an important risk factor; therefore, attention should be focussed on maintaining normotension in the peripartum period.

**Keywords** Cerebrovascular complications · Stroke · Risk factors · Pregnancy and puerperium

### Introduction

Cerebrovascular complications are uncommon in women of childbearing age. However, the literature review shows that the risk of stroke and cerebrovascular complications are increased in pregnancy and puerperium compared to the non-pregnant women [1]. The hypercoagulable state of pregnancy and puerperium is an important factor contributing to the risk of cerebral infarcts and several risk factors have been implicated, which can predispose a pregnant woman to cerebrovascular complications. The aim of this study was to analyze the incidence, possible etiological factors, pathology, clinical manifestations, brain CT scan features, treatment, and prognosis of non-hemorrhagic stroke and intraparenchymal hemorrhages occurring in association with pregnancy and puerperium.

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## Methodology

This is a prospective analytical study conducted at the Govt. Hospital for women and children, Chennai, from January 2006 to February 2008. During the above period, there were 39,211 deliveries and 26 women were diagnosed with various cerebrovascular complications. In these patients, clinical data including demographic characteristics, associated risk factors, neurological signs and symptoms and their evolution, results of laboratory investigations, fundus changes, and results of neuroimaging, and the outcome of these accidents were noted. By eliciting careful history and reviewing the records, risk factors for stroke prior to pregnancy, namely hypertension, diabetes mellitus, cigarette smoking, hypercholesterolemia, OC pill use, previous known cardiac disease, and APLA syndrome, were looked for. Obstetric data such as parity, antenatal care, gestational age at the onset of stroke, and the presence of complications like PET, eclampsia, anemia, and sepsis were noted. All patients were evaluated by the Neurophysician to assess the nature and severity of the neurological deficit. Patients were also examined for the presence of deep vein thrombosis of the legs.

Stroke was defined according to the definition of the WHO [2]. The following investigations were carried out on all patients: complete hemogram, platelet count, bleeding time, clotting time, prothrombin test, APTT, urine analysis, liver and renal function tests, fibrinogen levels, Electrolytes, screening for Antiphospholipid antibody syndrome, fundus examination, electrocardiography, and CT scan of the brain. Clinical findings were periodically reviewed for the progression or regression of the neurological condition. The discharged patients were followed up at 6 months and 1 year after stroke for residual neurological deficit.

## Results

The incidence of cerebrovascular complications in this study was 66 per 100,000 deliveries. The mean age at presentation was 22 years. Eighteen cases were (69 %) primigravida and eight (31 %) were multigravid women. None had prior history of diabetes, hypertension, renal disease, seizure disorder, OC pill use, or smoking. Two women were suffering from cardiac disease. Only two patients were attending the antenatal clinic regularly and the remaining 24 women were referred from other hospitals either with high BP or anemia or sepsis. Hypertensive disorders were seen in 19/26 (73 %) cases, and 13 of them (50 %) were admitted with either intrapartum or antepartum eclampsia. Two cases presented with severe pre-eclampsia, two with severe PET with HELLP syndrome, and another two suffered from mild pre-eclampsia. Among

these cases, the systolic BP ranged between 130 and 220 mm of Hg and the diastolic BP ranged between 90 and 160 mm of Hg. Five patients were suffering from mild to moderate anemia with a hemoglobin of 8–10 g%. Another two patients were suffering from severe anemia with a hemoglobin of 5 g%. One patient was referred with severe intrapartum sepsis following cesarean section. The cause of stroke remained undetermined in two patients.

Analyzing the occurrence of cerebrovascular events in relation to the gestational period and puerperium showed that two patients presented with neurological deficits in the third trimester. The first case presented at 37 weeks of gestation with an intense headache and quickly progressed to hemiparesis. She did not have any known risk factors. The CT scan showed massive intracerebral hemorrhage. The second case presented at 32 weeks of gestation with antepartum eclampsia, and progressed to hemiplegia with facial palsy the next day and the CT scan showed arterial infarcts in the left post cerebral artery territory. In the remaining 24 cases, the neurological complications manifested in the postpartum period. Cases of intracerebral hemorrhage (ICH) (3 cases) and arterial infarcts (4 cases) manifested early and were clustered within 5 days of delivery. Venous infarcts also occurred early and were clustered within 7 days of delivery (14 cases), but in 3 cases, neurological manifestations occurred after 10 days and in these cases, associated risk factors such as anemia and sepsis were also seen.

The most common presenting symptom was seizure and was seen in 24 cases (92 %). Intense headache was present in two cases (7.7 %) prior to the stroke. Fever with high temperature was seen in 3 cases (11.5 %) and one of them had intrapartum sepsis. 17 patients were at varying stages of altered sensorium, varying from semiconsciousness to an unconscious state. Three patients presented with psychotic behavior. Hemiparesis/hemiplegia was seen in 20 cases (76.9 %). In these cases, there were also associated neurological deficits such as facial palsy (2 cases), ophthalmoparesis (1 case), and Aphasia (1 case) and acute loss of vision with cortical blindness in 5 cases (19.2 %). Isolated facial palsy was seen in 6 cases. Fundus examination was reported normal in 15 cases (57.7 %), Grade II retinopathy in 5 cases (19.2 %), Grade III retinopathy in 2 cases (7.7 %), and papilloedema in 4 cases (15.4 %). In one case, unilateral retinal artery occlusion was suspected. Hemoglobin level was more than 9 g% in all cases, except two. These two cases had Hemoglobin of 5 g% on admission. Platelet count ranged between 1.5 and 2 lakhs in 24 cases. BT, CT, PT, and APTT were normal in all cases. Fibrinogen levels were in the upper limit of normal values in all cases. In 2 cases, severe pre-eclampsia was complicated by HELLP syndrome and the platelet count was less than one lakh. Within 48 h of the occurrence of the stroke,

CT scan imaging of the brain was done in all 26 cases. Intracerebral hemorrhage was diagnosed in four cases; in one case, there was evidence of ventricular bleed and in two cases mass effect was seen. Five cases were diagnosed as arterial infarcts. In 16 cases, a diagnosis of cortical vein thrombosis (CVT) was made. In one case, CT scan imaging was reported as normal. However, based on the clinical findings, a diagnosis of CVT was made. All cases were treated with antiedema measures with mannitol and Furosemide. Anticlotting measures with heparin and aspirin was given to those cases in whom ICH was ruled out by CT scan. Pre-eclampsia, eclampsia, anemia, and sepsis were treated as per protocol. Cases that developed cortical blindness showed improvement in 24 h and total recovery was observed in 7 days. In those cases with hemiplegia/facial palsy and aphasia, recovery was noted from day two onward. Four cases recovered within 48 h (19 %), 10 cases (47.6 %) recovered within 7 days, 3 cases (14.2 %) recovered within 14 days, 2 cases (9.5 %) recovered within 30 days, and one case (4.7 %) recovered in 6 weeks. At 6 months follow up, one patient still had residual lesion. Cases suffering from venous infarcts recovered faster and almost 100 % recovery was seen in 4 weeks, whereas in those suffering from arterial infarcts, paralysis was dense and took a longer time to improve.

There were five maternal deaths (19.1 %) in this study, four cases died due to intracerebral hemorrhage and one case died due to CVT.

## Discussion

Studies have shown that strokes develop in pregnant women more frequently than in non-pregnant women of same age [1]. Wiebers [3] estimated that pregnancy increases the likelihood of cerebral infarction to about 13 times the rate expected in non-pregnant women. Kittner et al. [4] reported that for either type of stroke, cerebral infarction and intracerebral hemorrhage, the relative risk during pregnancy and puerperium was 2.4. The reported incidence of pregnancy-related cerebrovascular complications varies in different parts of the world. Through surveillance study from 1956 through 1967, Cross et al. [5] reported the incidence of strokes as 5 per 100,000 deliveries. In a large population-based study in the USA, 2850 cases of pregnancy-related stroke were identified with a rate of 34.2 per 100,000 deliveries [6]. The incidence of cerebrovascular complications in our study was 66 per 100,000 deliveries, which is higher than the western reports. Srinivasan [7] also reported that CVT occurring in the puerperium is about 10–12 times more frequent in India than in western countries. The possible reasons for the high incidence in Asian countries could be due to coexistent

severe anemia and the local custom of fluid restriction during puerperium [8]. Another possible reason could be that, unlike the population-based studies, ours is a hospital-based study and being a tertiary referral center, more than 30 % of our patients are referral cases with pregnancy complications such as pre-eclampsia and anemia.

Many studies have shown that the risk of stroke is high in the postpartum period. Kittner et al. showed that for cerebral infarction, the RR during pregnancy adjusted for age and race was 0.7 (95 % CI .3 to 1.6), but it increased to 8.7 for the postpartum period (95 % CI 4.6 to 16.7). For ICH, the adjusted relative risk was 2.5 during pregnancy (95 % CI 1.0 to 6.4), but 28.3 for the postpartum period (95 % CI 13.0 to 61.4) [4]. Our study also showed that 24 of the 26 strokes occurred in the puerperium. During pregnancy and puerperium, there are extensive physiological, anatomical, and biochemical changes which can contribute to the pathogenesis of a stroke. The common risk factors reported in pregnancy and puerperium are pre-eclampsia/eclampsia, anemia, sepsis, choriocarcinoma, and congenital and acquired thrombophilias [9, 10]. The study by Kittner et al. [4] and the French collaborative study by Sharshar et al. [9] have found eclampsia to be an important factor associated with stroke. Kittner et al. [4] found pre-eclampsia or eclampsia in 24 % of women with cerebral infarction and 14 % of women with ICH, whereas the French study investigators found it on 47 % with cerebral infarction and 44 % with ICH [9]. In our study, 73 % (19/26) of the patients suffered from eclampsia/pre-eclampsia. Among these cases, in five of them there was also an associated mild to moderate anemia which could have contributed to the occurrence of stroke. Various reasons have been put forward for the occurrence of stroke in pre-eclampsia such as: higher cerebral perfusion, hemoconcentration, and activation of coagulation cascade [11, 12]. Eclamptic women are prone to develop ICH as a result of severe hypertension [9]. Witlin et al. [13] have shown that cerebrovascular malformations are seen in 20 % of patients with pregnancy-related ICH. Reports have suggested that reactive thrombocytosis in pre-eclamptic patients with HELLP syndrome may also contribute to postpartum thrombosis [14].

Anemia is also an important contributory factor for the development of cerebrovascular complications. In our study, 7 of the 26 cases (27 %) suffered from anemia; those with mild to moderate anemia also suffered from eclampsia/pre-eclampsia. Wiebers [3] points that anemia and hypotension during epidural anesthesia may predispose to cerebral events. The presence of any infection either localized or general has also been implicated as a cause of CVT [6]. In the study by Srinivasan [7], of the 135 cases with venous or arterial thrombosis, there was evidence of pelvic sepsis in 3 cases. In our analysis, only one case

presented with sepsis. Other etiological factors which have been implicated in the etiology of stroke are: the presence of anticardiolipin antibodies, and Hyperhomocysteinemia [15].

Reports from western countries have shown that most pregnancy-related infarctions are attributable to arterial occlusions [4, 5, 9]. However, arterial occlusion is less common in Indian studies. Based on clinical manifestations and Neuroimaging, arterial infarcts were diagnosed in five cases, which typically occurred in either the posterior or middle cerebral artery territory. Similar to our study, Srinivasan [7] also showed that arterial infarcts occurred only in 6 of the 135 women with stroke. In contrast, venous strokes are less common in the western population [5]. CVT during pregnancy and puerperium is a common entity in India [7]. Our study has also shown that, out of the 26 cases, 17 cases were diagnosed with CVT. The high incidence of CVT in the Indian population could be due to anemia, sepsis, and the custom of withholding fluid in the puerperium leading to dehydration. In CVT, symptoms are caused by the obstruction of cortical veins and superior longitudinal sinus. This results in impaired CSF absorption, causing raised ICT or obstruction of the draining veins resulting in cerebral infarction. Studies have shown that prognosis of ICH is much more severe than that of venous or arterial infarctions [9]. Even in our study, all four cases with intracerebral hemorrhage died. Srinivasan's [7] report stated that CVT occurred mostly in the second week of puerperium; however, it can be delayed by 3–4 weeks. In our study, ICH and arterial infarcts manifested early and were clustered within 5 days of delivery. CVTs were mostly clustered around the first week and few cases occurred in the second week also. James et al. [6] reported an overall fatality rate of 4.1 % for pregnancy-related stroke. In our study, the maternal mortality rate with stroke was 19 %, four were due to ICH and one was due to CVT. Patients with venous occlusion were very ill, features of raised ICT may be there and mortality is high, but those who survived had no significant disability. Patients with arterial occlusions were conscious with no signs of ICT and low mortality rate; but, neurological deficit often persists [7]. In our study, all patients with arterial occlusions survived and at the end of 6 months, residual lesion still persisted in one case. Among the 17 cases with CVT, there was one death, but in those who survived, there was quick recovery of the neurological deficit.

## Conclusion

Stroke occurring in pregnancy, though rare, is a serious complication which can lead to maternal death. In this

study, hypertension has emerged as an important risk factor for the occurrence of stroke; therefore, attention should be focussed on rapid control of hypertension and maintaining normotension in the peripartum period. In a country like ours, it is also important to correct anemia and avoid dehydration in the peripartum period. There should be greater awareness and liberal use of CT/MRI in those cases that are refractory to magnesium sulfate therapy, in those who presented with seizures in the puerperium, and in those cases presenting with stroke or loss of consciousness. After excluding ICH, early initiation of anticoagulant therapy can prevent further progression of thrombus and infarcts and will considerably reduce the morbidity and mortality.

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