

Research Article**Clinical Study of Etiology, Risk Factors and Outcome of Stroke in Pregnancy**G.V.Murali¹, M.Vijayasree², Y.Rama Koteswara Rao³, K. Vijay Kumar³, K. Ramachandra⁴¹Associate Professor, Department of Neurosurgery, Mamata Medical College & General Hospital, Khammam, India²Professor, Department of obstetrics, Mamata Medical College & General Hospital, Khammam, India³Professor, Department of Ophthalmology, Mamata Medical College & General Hospital, Khammam, India⁴Professor, Department of ENT, Mamata Medical College & General Hospital, Khammam, India***Corresponding author**

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Abstract: Stroke is the second leading cause of death of women even in the developed countries. Stroke associated with pregnancy has been long recognized and may partly be responsible for this increased incidence. Stroke related to pregnancy is associated with significant morbidity and mortality. Aim of the study was to characterize the subtypes of stroke associated with pregnancy and the puerperium, with emphasis on timing, etiology, risk factors, and outcome. It is a retrospective analysis of patients admitted to the neuro department over a period of 5 years from January 2009 to December 2013, with a diagnosis of stroke during pregnancy or within 6 weeks postpartum. Strokes were classified as ischemic (arterial or venous) or hemorrhagic (subarachnoid or intracerebral). All patients were investigated with at least a CT scan of the head, and most had MRI and/or cerebral angiography. 35 patients with a diagnosis of stroke were identified (21 infarctions and 14 hemorrhages). Of patients with infarction, 13 were arterial and 8 were venous. Nine of 13 arterial events occurred in the third trimester or puerperium. Seven of 8 venous occlusions occurred postpartum. An etiologic diagnosis was made in 7 of 14 patients with arterial territory infarction, including cardiac emboli, coagulopathies, and carotid artery dissection. Of patients with hemorrhage, 8 were subarachnoid and 6 were intra cerebral. The etiology was identified in 10 patients: 3 were due to ruptured aneurysms, 5 were associated with arterio venous malformations, and 2 were associated with disseminated intravascular coagulation. All patients with infarction survived, but 3 patients with hemorrhage died. In conclusion, the majority of strokes associated with pregnancy were arterial occlusions. Most presented during the third trimester and puerperium.

Keywords: Stroke, Pregnancy, Maternal morbidity, Mortality.

INTRODUCTION

Neurological disorders encountered during pregnancy are those common to reproductive aged women. Disorders like stroke and bells palsy are even more common in pregnancy. Stroke is the second leading cause of death of women in Canada and the United States [1, 2]. There is a higher incidence of stroke in young women between the ages of 15 and 35 years [3]. The American Maternal Mortality Collaborative reported cerebro vascular disease as the fifth cause of maternal deaths during 1980–1985 [4]. Many women with chronic neurological disorders become pregnant and have successful pregnancy outcomes. Conversely, neurological disorders do contribute to maternal mortality rates and there are specific risks with which the clinician should be familiar. Many women with chronic neurological disorders are diagnosed before pregnancy. In others, these symptoms appear for the first time in pregnancy and should be distinguished from pregnancy related complications. So, the present study was conducted to evaluate the retrospective analysis of patients diagnosed with stroke during

pregnancy and the puerperium who were admitted to the Mamata general Hospital between January 2009, and December 2013 over a period of five years, and to study the risk factors, etiology outcome of stroke in such patients.

MATERIALS AND METHODS

The total number of deliveries was determined from a review of obstetrical records and from the medical records department. Patients with a diagnosis of stroke during pregnancy and the puerperium admitted to the Mamata general hospital between January 2009 and December 2013 over a period of five years, were identified. The medical records were reviewed and the following data were abstracted: maternal age, parity, timing of presentation and presenting deficit, pregnancy-related risk factors for stroke (eclampsia or pre-eclampsia), and non-pregnancy related risk factors for stroke (hypertension, diabetes, hyperlipidemia, and tobacco use). A history of eclampsia or pre-eclampsia was noted if it appeared in the hospital chart. Information regarding investigations (neuroimaging,

cardiac investigations, hematologic assessment) was also abstracted. All patients had CT imaging of the brain. Most patients with infarction had MRI and cerebral angiography. All patients with hemorrhage, except 2 who died before investigations, were studied with cerebral angiography or had craniotomies. An etiologic diagnosis was made from the above investigations. Information regarding maternal and fetal outcome was abstracted if available. Because our hospital is a tertiary referral center, we attempted to distinguish between patients who resided in the area served by the hospital and patients referred for specialized obstetrical and neurological care by the private practitioners.

RESULTS

Fifty patients were identified with a possible diagnosis of stroke associated with pregnancy. After review of the medical record, 35 patients had a final diagnosis of stroke. Two patients were excluded from this analysis because of incomplete investigations. The remaining patients were excluded because of non stroke diagnosis, which included epilepsy, embolization for epistaxis, preceding neurological deficit, Bell’s palsy, cerebral abscess, delirium, neoplasm, and multiple sclerosis. The number of strokes per 100 000 deliveries was calculated for all patients and corrected for patients within the catchment area. These data are summarized in Table 1. Of the 35 patients with stroke, 21 were ischemic (13 arterial, 8 venous) and 14 were hemorrhages (8 sub arachnoid, 6 intra cerebral). Patient age, parity, etiology, and risk factors for each stroke sub type are summarized in TABLE 2. In patients with infarction, an etiologic diagnosis was made in 7 of 13 patients with arterial territory stroke and 3 of 8 patients with venous thrombosis. In patients with an identifiable etiology, only 1 abnormality was identified. In patients

without a known cause of stroke, vascular risk factors were identified in an additional 4 of 7 patients with arterial territory stroke. Three patients had 1 risk factor, and 1 patient had 2 risk factors. These included pre-eclampsia (2), tobacco use (2), and hypertension (1). In patients with venous thrombosis of unknown cause, 2 were also diagnosed with pre-eclampsia. Of patients with subarachnoid hemorrhage, 3 were due to aneurysmal rupture. The 3 aneurysms were identified as posterior communicating artery aneurysms. Intra cerebral hemorrhages were reported in the parietal and occipital regions in 4 of 6 patients; the other locations were frontal and cerebellar. Most arterial strokes presented in the third trimester and puerperium. All but 1 venous infarction presented in the puerperium. Patients presented with subarachnoid hemorrhage during each trimester and the postpartum period. Patients presented with intra cerebral hemorrhage after the first trimester. Patients presented with hemorrhage secondary to aneurysmal rupture during each trimester. Patients presented with bleeding from arterio venous malformations (AVM) after the first trimester. Bleeding as a consequence of disseminated intravascular coagulation (DIC) occurred postpartum. The outcome of patients with both infarction and hemorrhage was determined. All patients with infarction survived. However, 3 patients with hemorrhage (1 AVM, 2 unknown etiology) died during admission. Eight patients with infarction and 9 patients with hemorrhage presented before delivery. Of patients with infarction before delivery, there were 3 live deliveries, 1 miscarriage, and 1 termination. The outcome of 3 pregnancies was not available. Of patients with hemorrhage before delivery, there were 5 live deliveries, 3 deaths due to maternal death, and 1 termination.

Table 1: Frequency of Stroke Associated with Pregnancy

| Frequency | All strokes | Infarction | Hemorrhage |
|--|-------------|------------|------------|
| No. of events per 100 000 deliveries | 67 | 41 | 26 |
| Corrected no. of events per 100 000 deliveries | 26 | 18 | 8 |

Table 2: Baseline Demographic Variables

| Age, Yrs parity | All Patients (n=35) | Arterial infarct (n=13) | Venous thrombosis (n=8) | Subarachnoid Hemorrhage (n=8) | Intracerebral hemorrhage (n=6) |
|-----------------------|---|--|-----------------------------|---|--|
| Age, Yrs | 30(20-40) | 30 | 31 | 27 | 30 |
| Parity | 12 Primipara 20 Multipara 3 unknown | 4 primipara 9 Multipara | 3 primipara 5 multipara | 3 primipara 4 multipara 1 unknown | 2 primipara 3 multipara 1 unknown |
| Etiology | - | 6 unknown 4 cardiac 2 coagulopathy 1 large artery | 5 unknown 3 coagulopathy | 3 aneurysm 3 unknown 1 AVM 1 DIC | 1 unknown 4 AVM 1 DIC 1 unknown |
| Vascular risk factors | 3 preeclampsia 3 tobacco 1 hypertension | 3 preeclampsia | 1 tobacco | - | 1 preeclampsia 1 tobacco |

DISCUSSION

Till date, there is no proper consensus regarding the incidence of stroke associated with pregnancy. An early study in Rochester, Minn, reported an incidence of 3.5 ischaemic strokes per 100 000 population [5]. The incidence during pregnancy was reported to be 5 infarctions per 100 000 pregnancies in Glasgow, Scotland [6]. More recently, Sharshar *et al.* [7] reported an incidence of 4.3 non hemorrhagic strokes and 4.3 intra cerebral hemorrhages per 100 000 deliveries.

In the present study we report 69 strokes per 100 000 pregnancies. However, our hospital is a tertiary care referral center for neurology, neurosurgery, and obstetrics. The most common causes of the stroke in pregnancy in our study were gestational hypertension, pre eclampsia and obstetric haemorrhage. Migrain headache which was aggravated in pregnancy, sickle cell anaemia and thrombophilias which are very common in a tribal area near badrachalam which is situated near our centre were also the next common causes of stroke. The incidence of stroke in non pregnant women aged 15 to 44 years was reported as 10.7/100 000 women years [8].

After review of a series of reports in the medical literature, Wiebers [9] reported a 13-fold increase in the risk of stroke. This was subject to potential selection bias. More recently, in a population-based study of patients in Baltimore, Md, and Washington, DC, Kittner *et al.* [10] reported a relative risk of 0.7 of cerebral infarction during pregnancy. This increased to 8.7 during the postpartum period. Women with eclampsia will suffer symptomatic strokes from larger cortical infarctions. A study by Ramnarayan and Sriganesh and Singhal and colleagues in 2009 found that the reversible cerebral vaso constriction syndrome, also called peripartum angiopathy can cause extensive cerebral edema with necrosis and wide spread infarction with areas of haemorrhage. The relative risk of intra cerebral hemorrhage was 2.5 during pregnancy and 28.3 during the postpartum period. It has been long assumed that the majority of strokes associated with pregnancy were secondary to venous thrombosis. According to Wasay and co-workers, 2008 [11], in a 10-center study in the United States, 7 percent of cerebral venous thrombosis were associated with pregnancy. Even so, Cross, 1968; Lanska and Kryscio, 2000; Simolke, 1991, and all their colleagues [12] reported that pregnancy associated cerebral venous thrombosis is rare in developed – countries. Incidences range between 1 in 11,000 to 1 in 45,000 pregnancies. In the Nation wide in patient sample of more than 8 million deliveries, James and associates in 2005 [13] observed that venous thrombosis caused only 2 percent of strokes during pregnancy. But, according to Ehtisham and Stern in 2006, more than 100 cases have been documented.

In our study, of 21 patients with infarction, 8 were secondary to venous thrombosis. The diagnosis of venous thrombosis was confirmed by MRI in 6 patients and by angiography in 2. Although venous thrombosis can present in association with pregnancy, most infarctions are attributed to arterial occlusion. It has been recently reported that the risk is greatest during the postpartum period. In our study most patients presented in the third trimester and the postpartum period. Two patients were diagnosed with arterial dissection in the postpartum period. In prior studies, the most common identifiable causes of cerebral infarction reported in 2 recent studies are eclampsia and pre eclampsia. The mechanism by which this results in cerebral infarction is unknown. It is for this reason that pre eclampsia and eclampsia were considered risk factors instead of etiologic factors in our study. Cox and associates in 1988 studied, causes of embolism which included arrhythmias-especially atrial fibrillation, rheumatic valvular damage, or mitral valve prolapse. Finally emboli from infective endocarditis was considered as a cause of maternal mortality [14]. Smith and colleagues in 2008 [15] found that when congenital vascular anomalies bleed, half do so into the subarachnoid space and half are intra parenchymal hemorrhage with subarachnoid extension. The incidence of bleeding from cerebral AVMs probably is not increased during pregnancy according to Finnerty and co-workers, 1999 and Horton and associates, 1990 [16]. Thus, they are very uncommon, and in the study from Parkland Hospital, Simolke and associates) reported only one case in nearly 90,000 deliveries. Although some suggest the AVMs bleed with similar frequency throughout gestation, Dias and Sekar reported an increase with maternal age [17]. The identifiable causes of arterial territory infarction in our study included cardiac emboli, coagulopathy and arterial dissection. Arterial dissection was identified as the cause of stroke in 2 patients. In 1 patient there was dissection of the internal carotid artery. In the second patient coronary artery dissection resulted in myocardial infarction and subsequent stroke. Other reported causes have included pre-eclampsia, vasculitis, and cavernous angioma. An additional cause identified in our study was DIC. Five of our 14 patients had prior uneventful pregnancies. The patients in our series presented with hemorrhage secondary to ruptured aneurysms in each trimester. Most patients with hemorrhage from AVM presented in the second trimester. Although this is consistent with previous reports, the reason for this is unclear [18]. Cunningham in 2005 [19] reported that pregnancy – associated hemorrhagic strokes, are often due to chronic hypertension with superimposed preeclampsia. Intra cerebral hemorrhage has much higher morbidity and mortality rates than subarachnoid hemorrhage because of its location and also chronic hypertension is associated with Charcot-Bochard micro aneurysms of the penetrating branches of the middle cerebral artery.

Pressure-induced rupture causes bleeding in the putamen, thalamus, adjacent white matter, pons, and cerebellum. In the 28 women described by Martin and associates in 2005 [20], 50% of them died and most survivors had permanent disabilities. They underscored the importance of proper management for gestational hypertension-especially systolic hypertension-to prevent cerebrovascular pathology. Maternal mortality has been reported in association with intra cerebral hemorrhage. The reported mortality associated with subarachnoid hemorrhage is 27% to 40%. Three of our patients with intra cerebral hemorrhage died shortly after presentation. Hemorrhage was caused by AVM in 1 patient and unknown in the remaining 2. Death was secondary to herniation in 2 patients and cardiac arrest in 1 patient.

CONCLUSION

In summary, our study is an attempt to characterize the spectrum of cerebrovascular disease associated with pregnancy assessed at our institution over a five year period. Our patients had complete vascular, cardiac, and hematologic assessments. We recognize that over time, the complexity of investigations increased with technological advancement. Most of the strokes in our cohort were arterial infarction. The identifiable etiologies included cardiac emboli, coagulopathies, and arterial dissection. Most arterial territory and venous infarction occurred postpartum. Intra cerebral hemorrhages occurred during each trimester and in the postpartum period. All patients with infarction survived, but 3 patients with hemorrhage died. With recent advances in early diagnosis and prompt treatment decreases the maternal morbidity and mortality.

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