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Study of Clinical and Etiological Profile and Outcome of Cerebral Venous Thrombosis in Pregnancy and Puerperium in a Tertiary Care Hospital in Eastern India

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Abstract

Background: Cerebral venous thrombosis (CVT) is not uncommon in pregnancy and puerperium. We conducted a prospective study of 35 patients of CVT admitted in our department for a period of 1 year.

Results: Headache was the most common symptoms. 25 (71.43%) patients presented with headache. Hemiparesis was presenting symptoms in 6 (17.14%) cases. Seizure and diplopia were present in 5 (14.23%) patients each. Altered sensorium was observed in 4 (11.42%) cases. The predisposing factors were predominantly non-infective and included inherited thrombophilias like anemia, protein C and S deficiencies, hyperhomocystinemia.

Investigations: MR venography is the most definitive imaging modality and revealed lack of flow due to thrombosis in venous sinuses most notably in superior saggital sinus. CT Scans revealed delta sign, cord signs in few cases.

Treatment: Anticoagulation is the cornerstone of treatment. LMW Heparin was given in all patients for 14 days and was followed by oral anticoagulant.

Outcome: In our study the mortality was 5.7 % due to better obstetric care, advent of newer imaging techniques and increased sensitization towards diagnosis.

Key words: cerebral venous thrombosis; venography.

Introduction

Cerebral venous thrombosis (CVT) is any thrombosis occurring in intracranial veins and sinuses, which is a rare disorder affecting 5 persons per million per year with huge regional variation. Puerperal CVT is more common in India than western world. The prevalence is 4.5/1000 obstetric admission. Pregnancy and puerperium are the most prevalent prothrombotic states leading to cerebral venous thrombosis. The first description of CVT, appearing in the French literature in 1825, was by Ribes, in a 45 year old man who died after a 6 month history of severe headache, epilepsy, and delirium.[1] In 1957, Padmavati et al., for

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the first time from India, reported 15 cases of CVT in puerperium in an epidemiological study evaluating the causes of hemiplegia in 44 women.[2]

Aims & Objectives

GENERAL OBJECTIVES: To document demographic profile of antenatal and puerperal patients of CVT and document various modes of presentations of CVT in pregnancy.

SPECIFIC OBJECTIVES: To identify specific etiology, if possible and record outcomes during hospital stay in this group of patients and assess the neurological status of the study group before and after specific treatment both clinically and radiologically.

Materials & Methods

STUDY SETTING: Obstetrics & Gynecology in-patient department, IPGME&R and SSKM Hospital, Kolkata and Neuromedicine in-patient department, Bangur Institute of Neurology, Kolkata

STUDY DESIGN: This was a descriptive observational study done between March, 2018 and August, 2019 involving a short period (3 months) of longitudinal follow-up. Total 35 cases were included based on purposive sampling.

DEFINITION OF THE PROBLEM: Cerebral venous thrombosis (CVT), also called cerebral venous sinus thrombosis (CVST), is a cerebrovascular disease with diverse clinical manifestations that often affects women of childbearing age and prevalent in antepartum and puerperal period. It's most common clinical manifestations are headache, seizures, altered consciousness, and neurological focal signs on physical examination. CVT is treatable and has a good outcome, if detected early.

DEFINITION OF POPULATION: All antenatal and puerperial mothers having evidence of cerebral venous sinus thrombosis. CVT was confirmed by neuroimaging (CT head or MRV brain) and authenticated by radiologist.

STUDY VARIABLES: Women aged ≥ 18 years presented in antenatal or puerperial period who fulfilled the following inclusion and exclusion criteria and gave written consent to participate in this study.

Inclusion criteria: Antenatal or postnatal patients admitted with complaints of headache, impaired consciousness, seizures and focal neurological deficit.

Exclusion criteria: Known epileptic mothers, diagnosed case of eclampsia and pre-eclampsia, CNS infection, head injury.

Treatment: All patients were treated as per instruction of neurologist. Low molecular heparin was used in most of the cases. We used unfractionated heparin in complicated and critical cases. After 10-14 days of therapy, oral anticoagulants were started under guidance of neurologist. Patients were put on long term oral anticoagulation as per their etiology. Dabigatran or warfarin was used in most of the cases to prevent recurrence. Dabigatran has a specific benefit. Routine measurement of PT, INR is not required for Dabigatran.

Results:

Total 35 patients were included in our study.

Demographic profile:

Age: The mean age of presentation was 28.29 years of age with a standard deviation of 5.824. Minimum age was 19 years and maximum age was 40 years.

If we divide the population in subgroups, maximum patients were in the age group of 20-30 years. Total 22 (62.85%) patients were in this age group. 12 (34.29%) were in the age group of 31-40 years and 1 patient was <20 years age group.

Residence: Among our study population, 21 (60%) were from rural back ground and 14 (40%) were from urban background.

Obstetric parameters:

Parity: In our study population, 12 (34.3%) patients were multipara, 19 (54.3%) patients were primipara and 4 (11.4%) patients were primigravida.

Status of current pregnancy: During hospital admission for cerebral venous thrombosis, 30 (85.7%) patients were in puerperal stage and 4 (11.4%) patients were in 3rd trimester of pregnancy and one patient was in 1st trimester of pregnancy. Among the puerperal group, 22 (62.9%) patients presented within 1 week of delivery, 4 (11.4%) patients presented within 1-2 weeks and 2-3 weeks of delivery, each.

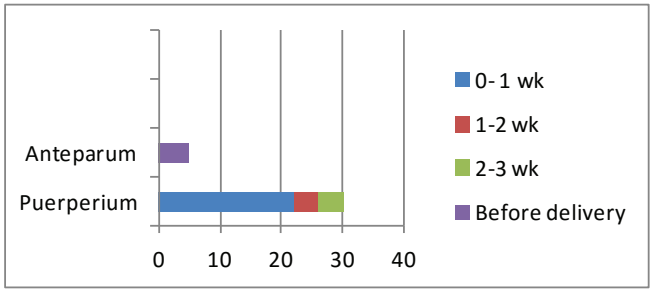

Figure 1: Onset of CVT

Mode of delivery: Among the 30 puerperal patients, 25 (71.4%) patients delivered normally through vaginal route and 8 (22.9%) patients had cesarean section. Out of the 5 ante-partum patients, one patient had cesarean section, 3 patients had normal vaginal delivery and one patient has not delivered yet. 33 patients were un-booked and 2 patients were booked.

Place of delivery: Among the 30 puerperal patients, 5 (14.3%) patients delivered at home and rest 25 (71.4%) patients delivered at hospital. Among the 5 ante-partum patients, 4 patients delivered at hospital and one patient yet to deliver.

Drug history: In our study population, 27 (77.1%) patients did not give history of OCP intake, but 8 (22.9%) patients had history of OCP intake during their lifetime.

Clinical presentation: Patients who were included in our study had various presenting symptoms. Headache was the most common symptoms. 25 (71.43%) patients presented with headache. Hemiparesis was presenting symptoms in 6 (17.14%) cases. Seizure and diplopia were present in 5 (14.23%) patients each. Altered sensorium was observed in 4 (11.42%) cases.

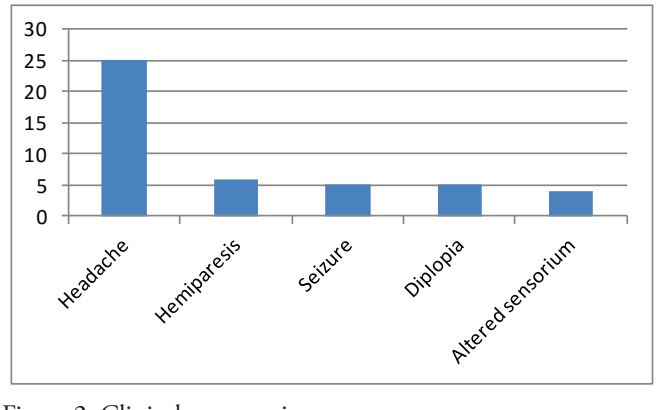

Figure 2: Clinical presentation

Clinical examination revealed the following findings. Papilledema was seen in 12 (34.2%) cases. Hemiparesis was seen in 7 (20%) cases, coma in 2 (5.7%) cases, 3rd nerve palsy in 6 (17.1%) cases, 6th nerve palsy in 2 (5.7%) cases and normal in 7 (20%) cases. We measured the functional status of the patient by modified Rankin scale. 7 patients had mRS 1, 16 patients had mRS 2, 7 patients had mRS 3, 3 patients had mRS 4 and 2 patients had mRS 5 status.

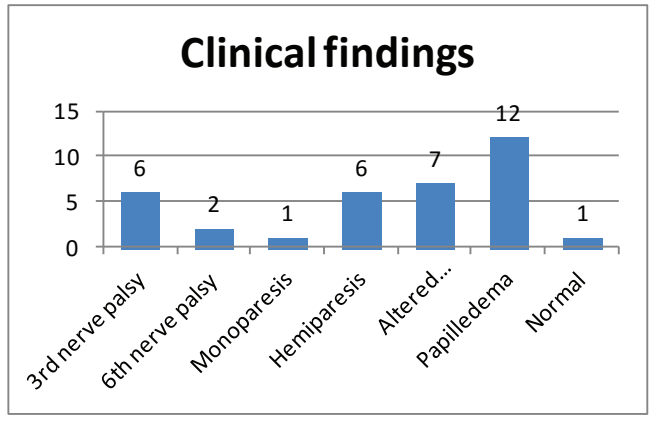

Figure 3: Clinical findings

Laboratory investigation: Complete hemogram analysis revealed normal analysis in 1 6 (45.7%) patients and anemia was detected in 12 (34.3%) patients. Anti-phospholipid antibody was present in 4 (11.4%) patients. Hyperhomocystenemia was detected in 7 (20%) patients and protein S deficiency was detected in 2 (5.7%) patients.

Radiological investigation: Among the study population, superior sagittal sinus (SSS) thrombosis was detected in 15 (42.9%) cases, transverse sinus (TS) thrombosis in 12 (34.3%) cases and cortical vein thrombosis was detected in 8 (22.9%) cases.

Contrast CT scan was done in all puerperal cases. Antepartum cases were excluded from CT scan. Haemorrhagic infarct was detected in 15 (51.4%) cases. Non- haemorrhagic infarct was detected in 8 (22.8%) cases. Delta sign was detected in 4 (11.4%) cases. CT scan was normal in 3 (8.6%) cases.

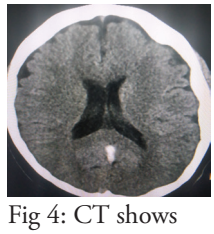

Fig 4: CT shows hyperdense venous sinus

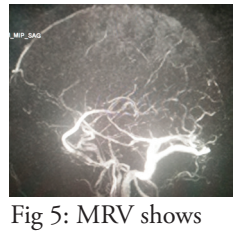

Fig 5: MRV shows thrombosed SSS

Treatment: Among our study population, 5 (14.3%) patients were treated with intravenous heparin due to their moribund state. All other, 30 (85.7%) patients were treated with low molecular weight heparin (LMWH).

Outcome: Out of the whole study population, 2 (5.7%) patients who presented during puerperium, died and 33 (94.3%) patients improved.

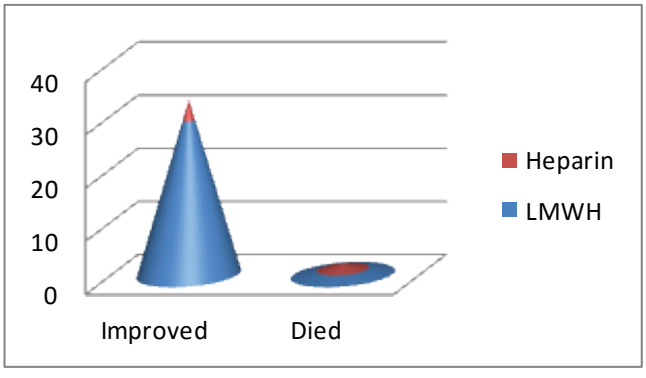

Figure 6: Treatment and outcome

We measured final outcome in modified Rankin scale at the end of 3 months. Total 31 (88.6%) patients had mRS 0-1, 2 (5.7%) patients had mRS 2 and 2(5.7%) patients died (mRS 6).

Relations between different parameters: There is no significant relation exists between various obstetric parameters and final outcome, but, significant relationship exists between presenting symptoms and clinical findings with outcome seen in our study. Paired sample T test between the functional status before and after therapy showed a statistically significant outcome (p value- 0.000).

Discussion

In the current study, majority of the cases (85.7%) were in the puerperal period, the results were consistent with the study conducted in India by Saroja AO.[3] Most of the affected patients (54.3%) were primipara, which is almost similar to other studies. The maximum occurrence of CVT, i.e. 74.3% was seen in the first two weeks of puerperium which is correlating with the series conducted by Srinivasan et al and Maru et al.4,5 Headache was the commonest symptom (71.43%) followed by seizures and altered sensorium.

In our study 6 patients presented with paralysis (17.14%). Similar results were seen in the studies by Pai et al and Narayan et al.[6,7] The incidence of coma in our study was only 5.7% compared to other case series from India that reported 43% to 93% of patients had an altered sensorium at presentation. The reason for this decrease is probably due to patients seeking medical help earlier in the recent times.

The fundus examination revealed normal fundus in 23 patients but 12 patients had signs of papilledema (34.2%). Papilledema may be seen in chronic cases or those with a delayed presentation but is less common in acute cases. All the above mentioned clinical profile correlated with the studies conducted by Srinivasan et al, Agostoni et al, Maru A et al.[4,5,8]

In our study, 34.3% cases of CVT had anemia. The association between anemia and CVT was explained by Coutinho J et al (2015) who suggested that iron deficiency anemia could result in thrombocytosis as a causal relationship.[9] Exaggerated hypercoagulable state of pregnancy, intravascular volume depletion due to edema, generalized endothelial injury and dysfunction favour thrombus formation. Anti-phospholipid antibody was present in 11.4% patients of our study population. Hyperhomocystenemia was detected in 20% patients and protein S deficiency was detected in 5.7% patients.

Physiological changes during pregnancy include increase in red cell mass and plasma volume with dilutional anemia. The plasma levels of protein S decline progressively during pregnancy while protein C levels remain unchanged. Antithrombin III levels are stable during pregnancy and rise after delivery. Acquired protein C resistance, high factor VIII, and factor V activity are found during pregnancy. Coagulation factors may be elevated during postpartum state up to 12 weeks, hence may not be reliable indicators of venous thrombosis. These changes during pregnancy and postpartum period confer a higher risk of venous thrombosis.

Diagnosis of CVT can be made from CT scans. However, sensitivity of CT scan is poor and shows direct signs of CVT in less than half of the cases. In our study, CT scan revealed hemorrhagic infarct in 51.4% of cases.

The American heart association/American stroke association 2011 scientific statement recommended magnetic resonance with T2 weighted imaging and

MR venography as the imaging test of choice for evaluation of suspected CVT. In our study, head CT was normal in 8.6% of cases.[10] MR venography revealed cerebral venous thrombosis in those 8.6% cases. So, MRV is of great diagnostic utility and these cases could escape detection if CT alone is used as the only neuro imaging modality.

Management of obstetric CVT is not different from that of CVT unrelated to pregnancy. Hence it includes supportive care, seizure control, measures to lower intracranial pressure, search and treatment of possible infection. To prevent further thrombosis, anticoagulation is the preferred treatment, currently. Of the 35 cases, 30 patients were treated with low molecular weight heparin and rest 5 were treated with unfractionated heparin. Use of heparin reduces the mortality as proven by similar studies like Srinivasan et al, Bousser and Ferro et al.[4,11,12]

Compared to arterial stroke CVT has favourable outcome. Most of our patients have recovered completely. Out of the 35 cases in our study, 2 patients in puerperium died. These two patients presented with seizure and coma. In the past, CVT was diagnosed mainly at autopsy and was considered to be a lethal disease with a mortality ranging from 30-50%.

Most CVT patients have a good prognosis. Approximately 80% of patients have mRS of 0–1, but they usually have residual symptoms and are often unable to return to their previous work. In our study the mortality was 5.7 % due to better obstetric care, advent of newer imaging techniques and increased sensitization towards diagnosis.

Conclusion

Cerebral venous thrombosis is not uncommon during pregnancy and puerperium. Adequate clinical suspicion, timely recognition, early diagnosis and prompt treatment can provide better prognosis and decrease maternal mortality and morbidity.

It is more during 3rd trimester of pregnancy and puerperium. Most cases of puerperal CVT presented with in the second week. Apart from hypercoagulable state, anaemia is the major causative factors. Headache was the universal symptom, and usually occurred in association with other symptoms like seizures, visual disturbances and focal deficits.

Majority of patients had hemorrhagic venous infarct on head CT. MRI brain with venography plays distinct role in those cases where CT scan is negative.

Low molecular heparin is effective in treating CVT in pregnancy and puerperium. Outcome is good if treatment starts early. Outcome also depends on the initial presentation. Mortality was low (5.7%) and most cases had excellent recovery.

REFERENCE

1. Ribes MF. Des recherches faites sur la phlebite Revue Medical Français et Etrangere er Journal de clinique del 'Hotel Dieu et de la Charite de Paris 1825;3:5.
2. Padmavati S, Gupta S, Singh B. A clinical study of 44 cases of hemiplegia in adult women. Neurol India 1957;5:59 65.
3. Saroja AO, Tapsi C, Naik KR. Cerebral venous thrombosis in women from Indian subcontinent. Journal of the Scientific Society 2017;44(1):20-25.
4. Srinivasan K. Cerebral venous and arterial thrombosis in pregnancy and puerperium: a study of 135 patients. Angiology. 1983;34(11):731-746.
5. Maru A et al : cerebral venous sinus thrombosis in pregnancy and puerperium , a prospective study, J assoc Physicians India 1998, aug; 46(8):748.
6. Pai N, Ghosh K, Shetty S. Hereditary thrombophilia in cerebral venous thrombosis: A study from India. Blood Coagul Fibrinolysis 2013;24:540 543.
7. Narayan D, Kaul S, Ravishankar K, Suryaprabha T, Bandaru VC, Mridula KR, et al. Risk factors, clinical profile, and long term outcome of 428 patients of cerebral sinus venous thrombosis: Insights from Nizam's Institute Venous Stroke Registry, Hyderabad (India). Neurol India 2012;60: 154 159.
8. Agostoni E. Headache in cerebral venous thrombosis. Neurol Sci. 2004;25(Suppl 3):S206-210.
9. Coutinho JM, Zuurbier SM, Gaartman AE, et al. Association between anaemia and cerebral venous thrombosis. Stroke 2015;46(10):2735-2740.
10. Saposnik G, Barinagarrementeria F, Brown RD, Jr, Bushnell CD, Cucchiara B, Cushman M, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/ American Stroke Association. Stroke J Cerebral Circulation. 2011;42(4):1158-1192.
11. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6(2):162-170.
12. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F, ISCVT Investigators. Prognosis of cerebral vein and dural sinus thrombosis: Results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke 2004;35:664-70.