

## ORIGINAL ARTICLE

### A STUDY OF THE CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH CEREBRAL VENOUS THROMBOSIS

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**ABSTRACT: INTRODUCTION:** Cerebral venous thrombosis (CVT) is an unusual cause of stroke that affects the young and is often missed or misdiagnosed. This study was undertaken to study the profile of patients who presented with CVT. **METHODS:** A cohort of 59 patients who presented to Sri Ramachandra Medical College and Research Institute, Chennai between June 2009 to September 2011 and were diagnosed to have CVT by neuro imaging were included in the study. Clinical and laboratory parameters were entered into a detailed questionnaire and patients were followed up during their stay in hospital. Data was analysed using SPSS software for Windows version SPSS 16.0. **RESULTS:** The mean age at diagnosis was 37 years. Headache was the most common symptom (86.4%) of patients followed by vomiting (44.1%) and seizures (42.4%). Papilledema was the most common sign in 37% of patients. Superior sagittal sinus was the most commonly affected. Hyperhomocysteinemia was the underlying etiological factor in 23%. 7 patients were in the pregnant and puerperal period. All patients were treated with anticoagulants. 2 patients died in hospital. **CONCLUSION:** CVT presents in the young, often with symptoms and signs of raised intracranial pressure. Response to therapy is better than with arterial stroke and there is a favourable outcome.

**KEYWORDS:** Cerebral venous thrombosis, Clinical features, Etiology.

**INTRODUCTION:** Cerebral venous thrombosis (CVT) is an uncommon neurovascular disease that has myriad symptoms, affects predominantly the young and is often missed. It has been prevalent since the early nineteenth century but recent advances in imaging techniques including widespread use of venography has resulted in an increase in the number of patients diagnosed. The current data suggests that it affects 5/million population annually and is responsible for 0.5-1% of all strokes.<sup>[1]</sup> It differs considerably from arterial strokes in the population affected, age at presentation, clinical features, treatment and outcomes. The etiological causes of venous thrombosis also differ from arterial risk factors such as diabetes mellitus, dyslipidaemia, hypertension etc. They are linked classically to the Virchow triad of stasis of the blood, changes in the vessel wall, and changes in the composition of the blood. This study was done to see the clinical and etiological profile of patients with cerebral venous thrombosis.

**METHODOLOGY:** This was a prospective study of a cohort of patients admitted to Sri Ramachandra Medical College and hospital, a tertiary care hospital located at Chennai, South India between June 2009 to September 2011 with a diagnosis of cerebral venous thrombosis. Approval was obtained from the hospital ethics committee and informed consent of the patients was taken. All patients were required to be more than 18 years of age. CVT was diagnosed on

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the basis of neuroimaging- either CT scan or MRI with a venogram. A detailed questionnaire was filled up including all the following data- age, sex, clinical symptoms and signs, evaluation including prothrombotic workup in specific cases, imaging, treatment and outcome till discharge from hospital or death. Patient was considered to have acute CVT if presentation was within 48 hours of onset of symptoms, sub-acute if between 48 hours to 30 days and chronic if duration was beyond 1 month.

Data was evaluated using SPSS software for Windows version SPSS 16.0. Software. Continuous variables were expressed as mean+/- standard deviation and discrete variables as number percentage.

**RESULTS:** A total of 59 patients were admitted during the study period with cerebral venous thrombosis. The mean age at presentation was 37 years with the youngest being 19 and the oldest 62 years. There was almost equal number of male and female patients with a ratio of 1.1:1 (31 and 28 patients) respectively (Table 1). Most of the patients presented with acute or sub-acute onset of symptoms with just 6 patients who had symptoms beyond 30 days. Headache was the dominant symptom in 86.40% patients with approximately less than half having vomiting or seizures. Focal loss of function or a visual problem was seen in roughly 25.4% of patients. Papilloedema was the most common finding on examination seen in 37.3% of patients. Hemiplegia, cranial nerve deficits, speech disturbances were present in 10, 6 and 4 patients respectively. Imaging revealed involvement of a single sinus in 25.4% of patients majority of them having superior sagittal sinus (10 out of 15). (Table 2) In those having more than one sinus involvement, superior sagittal sinus and transverse sinus were the two most frequently involved. 18 patients had block of 3 sinuses while one had involvement of 5 (superior sagittal sinus, transverse sinus, sigmoid sinus, internal jugular vein and cortical veins).

Etiological evaluation revealed hyperhomocysteinemia in 23%, polycythemia, protein S deficiency, dehydration in a small percentage. (Figure 3) Of the women patients, 7 were pregnant or in the puerperal period and 3 had a history of oral contraceptive use. In 37% of patients, no obvious cause could be detected. However procoagulation workup could not be done in 12 patients due to logistic difficulties. The clinical outcomes were good and only 2 patients died. 1 had all 5 veins blocked, both presented with a low Glasgow Coma Score, were on a ventilator and succumbed despite anticoagulant and supportive therapy.

**DISCUSSION:** The first case of CVT in India was reported by Padmavathy in 1957.<sup>[2]</sup> Earlier studies from India have reported a preponderance in women often in the pregnant and puerperal periods.<sup>[2,3]</sup> However recent studies have shown an equal distribution in both men and women.<sup>[4]</sup> Our study had an almost equal number of patients belonging to both the sexes with a slightly male preponderance though there were 7 patients who developed it during pregnancy or puerperium.

CVT is a disease of the young with 80% occurring in people less than 50 years of age.<sup>[5]</sup> The mean age in our case series was also 37 years. Acute or sub-acute headache was what brought 86% of patients to the hospital often also accompanied by vomiting or seizures. This is consistent with the findings of the largest prospective study of CVT, the International Study of Cortical Venous Thrombosis which showed that headache was present in 90% of patients often

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diffuse and building in intensity over days to weeks.<sup>[5]</sup> A simple fundus examination in the emergency room is probably the most important factor that would help decide the next step in management in view of the fact that papilloedema was the most common clinical sign seen in 37% of our patients. Most of the symptoms in CVT are linked to either raised intracranial pressure(ICP) or due to neuronal cell damage due to the venous infarction and or bleed.<sup>[6]</sup> The major diagnostic challenge is in identifying the subgroup of patients who have isolated headache and no papilloedema or focal neurological deficits.<sup>[7]</sup> Studies have demonstrated a delay in diagnosis of upto 7 days.<sup>[5]</sup> We too had nearly 62%patients who had no papilloedema or localising deficits. The common cranial nerve palsy that is seen is sixth nerve palsy probably due to the raised ICP.<sup>[5]</sup> Two of our patients also had evidence of facial nerve weakness and both had hemiplegia.

Compared to arterial stroke, focal deficits seem to be less common in CVT. Superior sagittal sinus(SSS) is the most commonly blocked sinus and usually presents with headache and raised ICP signs.<sup>[4]</sup> This was also seen in our patients where SSS was the commonest followed by transverse sinus. Deep cerebral venous involvement including vein of Galen, internal cerebral vein, straight sinus has been reported in 16% of patients.<sup>[8]</sup> We had only 10% patients with deep cerebral venous involvement.

Traditionally, the etiological factors looked for are acquired (surgery, trauma, pregnancy, puerperium, malignancy, use of oral contraceptive pills) or inherited ones (deficiency of protein C, protein S, antithrombin III, factor V Leiden mutation) etc. The most common etiological cause was hyperhomocysteinemia in 23% of our patients. However we were unable to find out an underlying cause in nearly 37% patients. 34.1% of patients in West who develop CVT have an underlying prothrombotic state.<sup>[5]</sup> Presence of protein S deficiency(Odds ratio of developing a CVT 12.5) and use of Oral Contraceptive Pills (Odds ratio of developing CVT 5.6) are the most common inherited and acquired prothrombotic etiological factors respectively.<sup>[6]</sup> Indian studies too found 12.3% of patients had an inherited prothrombotic state.<sup>[4]</sup> Amongst women, 7 patients developed CVT in pregnancy and puerperal period. In pregnant women, presence of hyperemesis gravidarum, infections, hypertension, increased maternal age and caesarean delivery have all been linked to higher rates of CVT.<sup>[9]</sup> Western data links OCP use especially when also associated with a hereditary prothrombotic factor deficiency with a very high incidence of CVT.<sup>[10]</sup> In India, OCP use is less and female sterilisation is the most preferred contraceptive method. That could explain the low number linked to OCPs (3) in our study.

Infections especially those in the parameningeal areas such as mastoiditis with a propensity to invade the brain or meninges have been associated with a high incidence of CVT in children.<sup>[11]</sup> However we had just one patient with a facial infection with spread causing cavernous venous thrombosis. The most common differential diagnosis include idiopathic intracranial hypertension, cerebrovascular arterial infarct or intracranial bleed, CNS infections, neoplasms and subarachnoid haemorrhages.<sup>[6]</sup> In fact, it is recommended that all patients with suspected idiopathic intracranial hypertension should undergo a venogram to exclude the possibility of CVT.<sup>[6]</sup> Improvement in imaging has resulted in increase in the number of patients being diagnosed. However plain CT Scan is abnormal in only 30% of patients. Hypersensitivity of the dural or cortical sinus, presence of cord sign, the dense triangle, and the delta or empty

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triangle sign, ischemia often with a bleed cutting across arterial territories are the signs looked for.<sup>[12]</sup> In MRI at a very early stage, thrombus is detected, and the occluded vessel appears isointense on T1-weighted images and hypointense on T2-weighted images. A few days later, the absence of flow void persists, but the thrombus becomes hyperintense.<sup>[13]</sup> Based on preliminary results, all our patients underwent venogram to delineate the involved sinuses. All patients were treated with either Intravenous heparin or subcutaneous Low Molecular Weight Heparin initially and then overlapped with oral warfarin. Warfarin dose was titrated to maintain an INR of between 2 to 3 and continued for 6 months in those with a definite antecedent cause and lifelong for those with inherited prothrombotic state. Previous studies have showed significant improvement in patients receiving heparin and study had to be stopped early in view of observed differences.<sup>[14]</sup> Anti-epileptic drugs were started in those who had seizures and antiedema measures in those who had cerebral edema. No surgical procedure was attempted on any patient. There is now a probable role for surgical decompression or endovascular thrombolysis in those not responding to conventional therapy.<sup>[15]</sup> 2 patients succumbed to the illness giving a mortality rate of 3.4% which is concurrent with other recent data from India.<sup>[4]</sup> The three main causes of death in CVT are 1) brain lesion itself, particularly when a large hemorrhagic infarct is present, causing herniation 2) intercurrent complications like sepsis, uncontrolled seizures and pulmonary embolism 3) underlying conditions like carcinoma, septicemia, leukemia and Paroxysmal Nocturnal Hemoglobinuria.<sup>[5]</sup>

**CONCLUSION:** CVT is a disease of the young that should be suspected in all patients with severe headache, fundus examination in the emergency room to look for papilledema should be done in all, imaging including venogram done and anticoagulation initiated with appropriate monitoring. Early identification and initiation of therapy results in favourable outcome.

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