



**A CLINICAL PROFILE AND OUTCOME OF CEREBRAL VENOUS SINUS
THROMBOSIS IN TERTIARY CARE TEACHING HOSPITAL**

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ABSTRACT

Background: Cerebral venous thrombosis (CVT) is an uncommon form of stroke, usually affecting young population. Clinical features of CVT are diverse, and for this reason, high degree of clinical suspect is mandatory to diagnose the conditions. The objectives of the study were to analyse the commonest clinical modes of presentation, possible etiologies, and to evaluate clinical outcome. **Methods:** This study was performed as a hospital based retrospective & prospective observational study at Tirunelveli medical college, Tirunelveli. All the patients admitted in our hospital with the diagnosis of CVT were subjected to neuroimaging techniques, fulfilling the study criteria were recruited by simple random sampling and data collected was analyzed by correlation studies. All patients hospitalized in between the period of 1 year (June 2018 to May 2019) with the final diagnosis of CVT (confirmed by imaging MRI/MRV OR angiography) to be included. All patients should be above 18 years of age. Patients who were initially diagnosed as CVT, But MRV/angiogram were normal; Patients below 18 years of age and known case of seizure disorder, migraine, cranial nerve palsies, and hemiplegic patients were excluded. **Results:** In our study, we found that CVT was more common in third decade of life. Puerperium was the common age group among female patients. In male patients, dehydration is the most common etiology. SSS thrombosis more common and involvement of more than one sinus is more common. Headache is the commonest complaint. Overall CVT had good prognosis and recanalisation was complete in most of the follow up cases. **Conclusion:** Suspicion and imaging were most crucial part of diagnosis. Prognosis of CVT mainly depend of early diagnosis and treatment.

KEYWORDS: CVT- cerebral venous/sinus thrombosis, CT – computed tomography, MRI – magnetic resonance imaging.

INTRODUCTION

Cerebral venous sinus Thrombosis (CVT) has been recognized since the early 19th century^[1] but still remains a diagnostic and therapeutic challenge. Cerebral vein and sinus thrombosis is rare compared to arterial stroke often occurs in young individuals.^[2] CVT may occur at any time from infancy to old age most reported cases were women in association with puerperium.^[3] Onset of symptoms may be acute sub acute or chronic. Cerebral venous infarction is the most serious consequence of cerebral venous thrombosis venous infarctions are often multifocal bilateral affecting both grey matter and sub cortical white matter.

Patient of CVT usually presents with headache, seizure, papilloedema, altered sensorium and focal deficits due to thrombosis of intracranial veins and sinuses resulting in hemorrhagic infarctions and raised intracranial tension.^[2] The above features are present in various combinations ranging from syndrome of raised intracranial pressure without localization to deep altered sensorium and dense hemiparesis. CVT forms a distinct

subgroup of cerebrovascular disease in India and is a leading cause of mortality in women of reproductive age group.^[3] In India, most of the cases are seen in post partum period in women, while alcoholism is a significant risk factor in males. Pangayara reported from India that CVT accounted for half of young stroke and 40% for stroke in woman. Cross et al^[4] noted: "Usually recovery is rapid and complete if patient survives the acute episode". Three fourth of cases of CVT in pregnancy and puerperium reported by him, survived with good recovery. However, in pre imaging era CVT had been diagnosed exclusively at autopsy and therefore thought to be always lethal. After introduction of heparin in treatment of CVT mortality has come down significantly and most of the recent studies^[5] reporting mortality < 20% compared to earlier studies reporting mortality between 30-50%. However outcome of CVT is highly unpredictable and it is not unusual to see dramatic recovery in deeply comatose patient and sudden worsening in conscious patients due to extension of thrombosis. With the advent of imaging modalities like CT scan and recently Magnetic Resonance Imaging

(MRI) and Magnetic resonance venography (MRV), the diagnosis of CVT has improved significantly. Due to multifactorial causation of this condition, it will be interesting to know whether different pathophysiological mechanisms are operating in different clinical settings. Although some patients with CVT present with complications, such as a stroke with focal neurologic signs or coma, many present with mild or nonspecific symptoms, such as isolated intracranial hypertension, presenting with headache and papilloedema. However, conversely to arterial stroke, scarce information exists on natural history and long-term prognosis of CVT. Based on this aim of our study is to identify the etiological spectrum of patients with cerebral vein thrombosis, also to attempt correlation between site of venous occlusion and clinical parameters. To evaluate the prognosis of CVT and the factors associated with poor outcome.

MATERIALS AND METHODOLOGY

This study was performed as a prospective observational study at Tirunelveli medical college, Tirunelveli. All the patients admitted in our hospital with the diagnosis of CVT were subjected to neuroimaging techniques, fulfilling the study criteria were recruited and data collected was analyzed by correlation studies All patients hospitalized in between the period of 1 year (June 2018 to May 2019) with the final diagnosis of CVT to be included. All patients should be above 18 years of age. Patients who were initially diagnosed as CVT, But MRV/angiogram were normal; Patients below 18 years of age and known case of seizure disorder, migraine, cranial nerve palsies, and hemiplegic patients were excluded. Patients were included in the study after obtaining signed informed consent.

A detailed proforma with the necessary information were prepared and details received from patients. Full and meticulous general and physical examination done for all the patients to find out any Focal signs, ICH /Papilloedema signs, Sensorial status. Glasgow coma scale (GCS) scoring was done on admission and during the clinical course; Follow up performed at 3 months, 6 months, at 12 months. For patients who were lost to follow-up, the condition on the day of hospital discharge was regarded as the final follow-up. We summarized the demographic data as mean and median. Fisher's exact test and multivariate logistic regression were used for analysis. IBM SPSS statistical software was used.

RESULTS

In our study a total of 100 patients were taken for study and 56 were male and 44 were female. Majority of patients were in second and third decade of their age. Patients were in above fourth decade of their age. 4 pts were less than 18 years of age. 4 female patients were between 19 and 20 years of age. The mean age was 30.18. The range was 12-76 years. Out of 44 female patients, 40 (87.5%) were puerperal and 4 (12.5%) were non puerperal CVT. Among 4 non puerperal cases, 1 case was diagnosed as fungal meningitis. 1 case was

diagnosed as HIV positive. one case had TB meningitis. Majority of patients (87) had duration of symptoms less than 30 days. A small number of patients (8) had symptom duration of less than 24 hrs. And 5 had symptoms present more than a month

Table 1: Mode of onset.

Mode of onset	Percentage
Acute (< 48 hours)	30%
Sub acute (day 3 – day 30)	65%
Chronic (> 1 month)	5%

Most of the men presenting with CVT had history alcoholism (42 patients) and some dehydration. Most of the female patients got puerperal CVT (40 patients). In non puerperal women infection is the most common cause, with diabetes as risk factor. In 20 patients risk factor could not be identified. Rheumatologic evaluation was also done if needed. Also we found 11 patients were smokers. 6 were pan chewers. All these factors contribute to hypercoagulable state. PCOD, OCP pills use the major risk factors identified which were present in 10 out of 100 cases of each in CVTS. CSOM were identified as a risk factor in 6 cases. Two patients had history of CSF leak as the only etiology.

Table 2: Etiology.

Etiological Spectrum	Percentage
Systemic disease	10
Elevated serum homocystine	6
SLE	2
OCP	10
Dehydration	67
Polycythemia	19
Alcohol	51
ANCA	4
Post partum	31
Infective	12
OCP ,Protein S	2
Unknown	20

Majority of patients were in normal sensorium while 30 patients were drowsy. Glasgow Coma Scale (GCS) score was available in all patients. 15 of patients had GCS less than 5 and all of them are immediately intubated or referred from other centers in intubated state. Out of 100 patients 83 patients had headache at the time of presentation, 55 patients had focal deficits, and 71 patients had seizures and among 12 had generalized seizures, Focal seizures in 30 patients and status epilepticus in 9 patients. Facial nerve involvement present in 12 patients. Other cranial palsies were present in 18 patients.

Table 3: Distribution of Patients According To Clinical Features at Presentation.

FOCAL SIGNS	
No focal signs	45
Hemiplegia	36
Hemiplegia with global aphasia	6
Quadriplegia	2
Agraphia ,alexia	2
Cerebellar signs	5
Global aphasia	2
Visual field defects	2
PAPILLOEDEMA	
Absent	46
Present	54
SEIZURES	
No seizure	29
Generalized seizures	31
Partial seizures	30
Partial seizures & Status epilepticus	9
Partial & secondary generalized seizures	10
CRANIAL NERVE PALSY	
No	76
3,4,6,7	2
6	14
6,7	4
UMN FACIAL PALSY	
Absent	88
Present	12
HEADACHE	
Absent	10
Present	83

Thirty eight patients were subjected to CSF analysis. CSF analysis done whenever there was suspicion of meningitis. Among 38 patients 16 were normal and abnormality seen in rest 22 patients with pleocytosis being the maximum. Two patients had TB meningitis with low sugar and high protein content and ADA positive. Two patients had Fungal meningitis with carvenous sinus thrombosis. Two patients had HIV infection.

CT/MRI FINDINGS

Infarction was present in 66 of them out of which 57 had hemorrhagic infarction. 9 patients had non-hemorrhagic infarction. 45 patients had cortical infarction while 5 had deep infarction. One patient had evidence of both cortical and deep infarction. Other than infarction, abnormalities noted on CT scan were mass effect & diffuse edema in among 32pts. 10 pts had cord sign and 7 had empty delta sign. Lesions in more than one cerebral lobe are more common than single lobe involvement. Temporo-occipital lobe lesion was more commonly involved. Among single lobe involvement also temporal lobes were more common. No lesion is seen in 10 patients.

Table 4: CT findings.

Area of involvement	Ct Findings
No lesion	10
Frontal lobe lesion	11
Fronto temporal lobe lesion	2
Fronto temporoparietal lobes lesion	2
Frontal & occipital lobes lesion	8
Frontal & parietal lobes lesion	11
Temporal lobe lesion	12
Temporo occipital lobes lesion	18
Temporo ,parieto occipital lobes lesion	2
Temporoparietal lobes lesion	4
Occipital lobe lesion	6
Occipital & parietal lobes lesion	10
Parietal lobe lesion	2
Diffuse edema	2
Total	100

MRV FINDINGS

Superior sagittal sinus (the commonest sinus involved) was involved in 61 patients, (isolated SSS in 7 patients). Total involvement was seen in 11 patients while in other patients anterior, middle and posterior parts involved with various combination of other sinuses. Transverse sinus was the next most common sinus involved 51 patients, (isolated in 4patients) Followed by sigmoid sinus present in 22 pts. Superficial venous system was involved in 5 pts (isolated in 2Pts) while deep venous system was involved in 5pts. Majority (89 pts) of patients had combination of sinuses and veins involvement, 11 pts had only isolated sinus involvement.

EEG abnormality is present in 20 pts, normal in 56 pts, focal slowing & generalized slowing was the most frequent abnormality, 1 pts had PLEDS, 54 pts had control of SZs with single AED, where as pts 8 required 2 AEDS. And 38 patients don't need AED measures.

All most all the patients received heparin. 88 of pts received unfractionated heparin, 12 pts received LMWH.IIH type of presentation were received LMWH. 1 pts DAVF underwent embolization. 5 patients underwent decompression craniotomy. Mechanical ventilator support was needed in 15 patients and 6 patients got good prognosis.

Correlation with etiology showed no constant pattern except that lateral sinus isolated involved in Mastoiditis. Correlation with mode of onset showed no difference in onset. No significant difference between presence of various sinuses and venous system the presence and location of infarction. when cortical veins are involved patients were presented with seiuzures and have intracranial hematoma than when only sinuses were involved.

Overall outcome of the CVT is good. Among 100 patients only 9 deaths occurred. Mostly due to very late

referral from other centers because of 'non suspecting' the CVT. Early diagnosis is the key factor for good prognosis in CVT. Early management with heparin is resulted in very good prognosis.^[1] All the patients who died had multiple Sinus thrombosis – mostly deep vein like cavernous sinus. And poor GCS at the time of admission is directly related to poor outcome. Among two fungal meningitis patients, none of them recovered. In HIV patient's mortality is 100%. In CVT due to head trauma, 1 death among 2 patients and had 50% mortality. In puerperal women, 4 deaths among 44 patient and had 9.09% mortality.

DISCUSSION

Cerebral venous thrombosis is condition characterized by thrombosis of intracranial veins and sinus which results in parenchymal damage and rise in intracranial pressure. Radiological hallmark of this condition is thrombosis of intracranial sinuses and veins with haemorrhagic infarction and edema with or without evidence of herniation. In this study, total 100 patients with Radiological features of cerebral venous thrombosis were evaluated. Only 50 patients were followed up over a period of 1 year. 56 out of 100 patients were male and remaining was female. This study of 100 patients with CVT cannot give precise information about the real incidence of the disease and cannot make any generalization of the results to whole country. It has been suggested that the incidence of CVT was higher in males. This was not confirmed in the present series, in which Male:Female ratio is 56: 44. This data is not consistent with previous Indian studies viz. Bansal et al.^[6], Srinivasan et al.^[7] High proportion of post partum CVT patients was also observed by Cantu et al.^[5] from Mexico with similar socio-demographic characteristics and economic status of the patients as in India due to referral bias. This finding of high proportion of CVT cases was not replicated in some other studies viz. Deschiens et al.^[8] and Daif et al.^[9] The possible explanation may be that the etiological factors as well as clinical profile of CVT is in this part of the state different compare to other parts of India More than half of the patients of CVT evaluated were in the second and third decade of their age. The mean age of the patients was years 30.15 similar to earlier studies from India.

However, it confirms the fact that the frequency of septic CVT (12/ 100) has markedly declined with the advent of antibiotics. It also confirms the role of oral contraceptives found as the only aetiologic factor in 5 of our patients. This has now led us, as many others to stop oral contraceptives and promptly look for CVT in women presenting with any of the neurological manifestations described in this study, particularly persistent headache, focal deficits or seizures.

In the present study in addition to conventional risk factors Dehydration (65% among male patients), hyperhomocysteinemia(6%), CSF leak (4%), OCP pill use (10%) are significant risk factors, 24% of patients had

Anemia, whether this is a reflection of high incidence of anemia in Indian population particularly in pregnant females or anemia is a real risk factor needs further evaluation. In 20/100 cases, no cause could be found, however complete etiological workup could not be completed.

Headache with or without vomiting (82%), remains the main presenting complaint of the patients. The present study was comparable with most other studies like Neki et al.^[11] with 85.5%, Daif et al.^[9] with 82% and Mehta et al.^[10] with 77.8%. Second most common complaint was seizures (71/100), then altered sensorium (65/100) and Focal deficits (55/100). Papilledema was present in 54 of our cases, was slightly more frequent than in other series: were the major clinical features noted at presentation. Similar findings were noted in the earlier studies. The clinical presentation could be summarized in 3 main patterns, each of them simulating another neurological disease. The most frequent and homogeneous one was the progressive onset of signs of intracranial hypertension corresponding to the "Benign intra-cranial hypertension" or "pseudo-tumor cerebri" syndromes, confirming that sinus thrombosis in 54 % cases these syndrome should not be diagnosed purely on clinical, CSF and CT scan findings without a good quality CT and MRV to rule out the possibility of sinus thrombosis. Other less common presentations are headache of sudden onset simulating subarachnoid hemorrhage (1 patient). It is therefore clear that CVT has no single clinical presentation and this is why it is necessary to systematically contemplate this diagnosis in order not to overlook it.

Present series most of the patients had good outcome, recanalisation in repeat MRI also achieved. Several reports have emphasized the importance of EEG changes in CVT, the most common pattern being a severe generalised slowing more marked on one side with frequent epileptic activity. 40 in the present series, EEG abnormalities were less severe and they were present in 38 % of cases. Its main interest was to show in a number of patients with focal symptoms a generalized slowing indicating a more diffuse lesion than was clinically suspected. This, however, is in no way specific of CVT. single case showed PLEDS The present series confirms the fact that isolated single sinus involvement was less common than multiple sinuses involvement, in isolated sinus most frequently involved are SSS and LS Thus in most cases, occlusion involved at least two sinuses or sinus and cerebral veins. Among these, cortical veins were affected slightly more commonly than the deep venous system. These frequent associations probably explain, at least partly, why no good clinico-radiological correlations could be established.

Before the introduction of angiography, CVT was diagnosed at autopsy and therefore thought to be most often lethal. In early angiographic series, mortality still ranked between 30% and 50% but in more recent series,

it was between 25% and 30% and in our study, it was only 9%. Multiple reasons can explain this decrease, the main one being probably that it is now possible to diagnose "benign" forms of CVT with minimal symptoms and spontaneous recovery. Another reason is that septic thrombosis has, since the use of antibiotics, become both far less frequent and severe. It is also that the introduction of anticoagulant treatment early in the course of the disease has improved the outcome. Two kinds of sequelae are encountered: blindness /fieldcut due to optic atrophy/cortical infarcts which should be prevented by early treatment, and focal deficits, usually motor, sometimes associated with epilepsy. Seizures are more frequent when the lesion is anterior to the central sulcus and in patients who have focal deficits. Most of patients presented with seizures were well controlled with single AED.

While the overall aim of treatment for CVT is to improve outcome, the immediate goals treatment for CVT are to recanalize the occluded sinus/vein. To prevent the propagation of the thrombus, namely to the bridging cerebral Veins. To treat the underlying prothrombotic state, in order to prevent venous thrombosis in other parts of the body, particularly pulmonary embolism, and to prevent the recurrence of CVT.

The main treatment option to achieve these goals is anticoagulation, using either heparin or low molecular weight heparin (LMWH). Early anticoagulation: Based upon available published data and guidelines, AHA/ASA guideline recommends the anticoagulation with subcutaneous LMWH or intravenous heparin for adults with symptomatic CVT who have no contraindication. The presence of hemorrhagic venous infarction is not a contraindication for anticoagulant treatment in CVT. 2 studies evidence suggests that subcutaneous LMWH is more effective than unfractionated heparin (UFH), and is at least as safe. Therefore, AHA/ASA suggests subcutaneous LMWH unless the patient is clinically unstable, or invasive interventions such as lumbar puncture or surgery are planned, or there is a contraindication to LMWH, such as renal failure.

Most of the pts who were followed up had re canalized the occluded veins. Only one pt expired in acute phase, Only 1 pt presented with recurrent CVT, sequelae were both more frequent in patients with focal symptoms than in patients with benign intracranial hypertension. The outcome was otherwise most unpredictable: some acute cases, even with coma, made a remarkably rapid and complete recovery whereas chronic cases often recovered more slowly and with more frequent sequelae. It is apparent from the study of literature and from the present series that the natural history and prognosis of CVT are highly variable. In this study, attempt was made to correlate the clinical profile with the topographic Radiological substrate like involvement of superficial / deep venous system or the pattern of infarction. There was no significant correlation to evolve a pattern of

diagnostic significance, correlating with radiological findings. However predictably, patients with deep venous system involvement and having ganglionic infarction had significantly less incidence of seizures. Patients with involvement of SSS had higher incidence of seizure and lower incidence of headache than those who didn't have SSS involvement. As most of the patients had extensive involvement of cerebral sinovenous system, contribution of degree of involvement of anatomical structures to a particular clinical profile cannot be reliably predicted. For example, high incidence of seizures in patients with SSS involvement may be attributed to the thrombosis from SSS spreading to cerebral veins causing cortical lesions and seizures but when a group of patients with only cerebral venous thrombosis without any sinus thrombosis was analyzed, seizure incidence was not high. Similarly patients with papilloedema did not differ in pathologic Radiological findings when compared to the patient group without papilloedema.

CONCLUSION

CVT is an important and treatable cause of the stroke; risk factors like hyperhomocystenemia, OCP use, alcoholism, procoagulant state are increasingly recognized in addition to the conventional risk factors like postpartum state. Procoagulant state and infections are the most common predisposing factors for cerebral venous thrombosis in this study. Prognosis of CVT predominantly determined by early suspicion, diagnosis of CVT and starting early management with anticoagulation treatment. Most of the patients who were followed up had recanalisation of the occluded veins. Complete recanalisation achieved in 88% of the cases. One patient had persistent occlusion and presented with recurrent CVT. Imaging plays a key role in diagnosing cerebral venous thrombosis, a condition that can be mimicked by several other neurological entities. The most sensitive diagnostic modality of choice is MRI with MR venography.

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