

# A Study of 50 Cases of Cerebral Venous Sinus Thrombosis

Mugundhan Krishnan<sup>1</sup>, Murugapandian Nagarajan<sup>2</sup>

<sup>1</sup>Associate Professor in Neurology, Government Kilpauk Medical College, Chennai, India.

<sup>2</sup>Senior Assistant Professor in Neurology, Government Kilpauk Medical College, Chennai, India.

Corresponding Author: Murugapandian Nagarajan

## ABSTRACT

**Background:** We undertook this study to analyze the demographic profile, frequency of different clinical features, risk factors, and prognostic outcome in patients suffering from cerebral venous thrombosis in our institution.

**Methods:** We performed a retrospective descriptive-analytical study in which 50 patients with cerebral venous-sinus thrombosis, who referred to Department of Neurology, Government Kilpauk Medical College from January 2017 to March 2019, were included, and their demographic, etiologic(risk factors), clinical, radiological and prognostic characteristics were evaluated.

**Results:** Out of 50 patients, there were 11 males (22%) and 39 females (78%); age ranged from 14 years to 72 years; headache was the most common symptom in 48/50 (96%), followed by paresis 23/50 (46%), seizures 22/50 (44%), papilledema 19/50 (38 %), mental status disorder 15/50 (30%), and aphasia 9/50 (18%). In majority of the patients 26 (52%), Pregnancy or Puerperium was the risk factor. The most common sinus involved was superior sagittal sinus(n-32), followed by almost equal involvement of transverse and sigmoid sinuses(n-29).Poor prognostic factors at the time of admission were stupor or coma (P=0.001) and parenchymal with or without subarachnoid hemorrhage in first CT scan.

**Conclusion:** Sinus thrombosis remains a diagnostic challenge and a potentially disabling or lethal disease, but improved diagnosis by recent advances and treatment now result in an excellent outcome for most patients.

**Key words:** Cerebral Venous Sinus Thrombosis; Pregnancy and Puerperium; Superior Sagittal Sinus

## INTRODUCTION

Cerebral venous-sinus thrombosis (CVST) is a potential life threatening condition that requires rapid diagnosis and urgent treatment which usually affects young to middle aged people. The outcome of patients with cerebral venous sinus thrombosis may vary from complete recovery to permanent neurological deficits, as a natural course of the disease. In 1957, Padmavati et al., for the first time from India, reported 15 cases of CVT in puerperium in an epidemiological study evaluating the causes of hemiplegia in 44 women.<sup>[1]</sup> In the late 1970's, hospital-based

series from Northern India documented CVT in a frequency of 4.5/1000 obstetric admissions. An angiographically proven study reported that 50% of the total cases of stroke in young women were related to pregnancy and puerperium and 95% of them were due to CVT.<sup>[2]</sup>

It has been thought that the incidence of CVT may be more in India compared to the western countries. This was probably due to the reporting of many large series of puerperal CVT from India in the 70's and 80's.<sup>[3]</sup> But, due to the lack of any population-based study or nationwide multicentric hospital-based studies, the

exact incidence of CVT in India is still not known. There have been a few epidemiological studies from the western countries trying to determine the incidence of CVT. A well-designed cross-sectional epidemiological study performed in the Netherlands had shown an incidence of 1.32/100,000/year.<sup>[4]</sup>

## **MATERIALS AND METHODS**

We performed a retrospective descriptive-analytical study in which 50 patients with cerebral venous-sinus thrombosis, who referred to Department of Neurology, Government Kilpauk Medical College from January 2017 to March 2019, were included, and their demographic, etiologic(risk factors), clinical, radiological and prognostic characteristics were evaluated. We have enrolled 50 patients with these inclusion criteria: (i) MR Venography showing cerebral venous sinus thrombosis; (ii) Age  $\geq$  13 years. Informed consent was taken from them. Detailed medical history including: Chief complaints, Origin, duration and progress, Past history particularly hypertension, IHD, DM and stroke and other, Family history, Personal history, menstrual history and obstetric history for women, Drug history – particularly in women for consumption of oral contraceptive pills taken. In all patients apart from vital data and detailed systemic examinations particularly of cardiovascular and central nervous system including fundus examinations done systematically. Routine blood investigations like Complete Blood count, Random blood sugar, urea, serum creatinine, and serum electrolytes were done on enrollment. Other specific investigations like PT with INR and aPTT, Chest X-Ray and X-Ray paranasal sinuses, ECG standard 12 leads, 2D Echo with colour Doppler, USG abdomen and pelvis, EEG in patients with seizures, Factor V leiden, Antithrombin III, Protein C and Protein S, Serum Homocysteine, Anti-phospholipids antibodies, ANA, Neuroimaging in form of MR Venography for confirmation of diagnosis and for etiological evaluation

carried out. Statistical Analysis: Findings were analyzed using Statistical Package for Social Sciences (SPSS software version 11.5). The data are reported as mean $\pm$ SD for quantitative variables, and as count and percent for qualitative variables. Chisquare test was used to analyze qualitative findings. A P value of  $\leq 0.05$  was considered statistically significant.

## **RESULTS**

### **Sex wise distribution**

Fifty patients (n = 50) were included with evidence of dural venous sinus thrombosis. Out of 50 patients, there were 11 males (22%) and 39 females (78%) as shown in Table 1.

### **Age wise distribution**

Age ranged from 14 years to 72 years. Out of 50 cases, 7 (14%) belonged to 13-20 years age group, 23 (46%) belonged to 21-30 years age group and 8 (16%) belonged to 31-40 years age group [Table 2]. 8 patients belonged to  $>51$  years age group.

### **Clinical presentation**

Headache was the most common symptom in 48/50 (96%), followed by paresis 23/50 (46%), seizures 22/50 (44%), papilledema 19/50 (38 %), mental status disorder 15/50 (30%), and aphasia 9/50 (18%). 12% of patients had sensory symptoms. Seven patients (14%) presented with coma as given in Table 3.

### **Risk factors**

In majority of the patients 26 (52%), Pregnancy or Puerperium was the risk factor. Cause was not identified in 20% (n-10) of patients. Infections and Oral Contraceptives were found in 5/50 (10%) each, genetic thrombophilia in 3/50 (6%), and Acquired prothrombotic condition in 2 (4%). In four cases (8%), there were multiple predisposing factors as shown in Table 4.

### **Duration of symptoms**

Most of the patients presented with more than one symptom. 19/50 (38%) patients presented with acute symptoms within seven days, 15/50 (30%) within 14 days,

and 13/50 (26%) within 30 days. 3 patients presented late after 30 days as given in Table 5.

**Site of occlusion in MRV**

In present study, the most common sinus involved was superior sagittal sinus(n-32), followed by almost equal involvement of transverse and sigmoid sinuses(n-29). The deep venous system was affected in six (12%) patients, and isolated cortical vein involvement was noted in 4% of cases. Most of the patients had involvement of more than 1 sinus. Commonest association was noticed between superior sagittal sinus and transverse or sigmoid sinuses. Thrombosis of deep venous system was least observed as given in Table 6.

**Prognostic factors:**

In this study 54 % of patients had complete recovery [Modified Rankin Scale (MRS): 0-1] on discharge. About 14 % of patients were partially recovered and independent (MRS: 2), while 22 % of patients had partial recovery but with dependence (MRS: 3-5). Death had occurred in 10 % of cases (Table 7). Poor prognostic factors at the time of admission were stupor or coma (P=0.001) and parenchymal with or without subarachnoid hemorrhage in first CT scan (P=0.005).

**Table-1: Incidence of cerebral venous sinus thrombosis according to Sex**

Sex	Number of Cases	Incidence	Male: Female
Male	11	22	1:3.5
Female	39	78	

**Table-2: Incidence of cerebral venous sinus thrombosis according to age group**

Age Group (Years)	Number of Cases			Percentage
	Male	Female	Total	
13-20	0	7	7	14
21-30	2	21	23	46
31-40	2	6	8	16
41-50	3	1	4	8
>51	4	4	8	16

**Table-3: Clinical presentation**

Neurological feature	Number of Cases	Percentage
Headache	48	96
Seizure	22	44
Papilledema	19	38
Aphasia	9	18
Paresis	23	46
Sensory symptoms	6	12
Mental status disorder	15	30
Coma	7	14
Visual symptoms	6	12

**Table4-: Incidence of different risk factors**

Etiology	Number of Cases	Percentage
Pregnancy or Puerperium	26	52
Genetic Thrombophilia	3	6
Acquired prothrombotic condition	2	4
Oral Contraceptives	5	10
Infection	5	10
Malignancy	2	4
Cause not identified	10	20
Multifactorial	4	8

**Table-5: Duration of symptoms at the time of admission**

Duration of symptoms	Patients	Percentage
0-7 Days	19	38
8-14 Days	15	30
15-30 Days	13	26
>30 Days	3	6

**Table-6: Site of Occlusion in MRV**

Sinus Involved	In combination	In Isolation
Superior Sagittal Sinus Thrombosis	32	10
Transverse/Sigmoid Sinus Thrombosis	29	9
Deep Venous system Thrombosis	6	2
Isolated Cortical Vein	-	2

**Table-7: Outcome of patient on discharge according to Modified Rankin Scale**

Modified Rankin Scale	No. of Cases	Percentage
0	12	24
1	15	30
2	7	14
3	5	10
4	4	8
5	2	4
6	5	10

**DISCUSSION**

In this study, 50 patients with dural sinus thrombosis were studied on the basis of MRI and MRV. Out of 50 patients of CVST, 11/50 [22%] were males and 39/50 [78%] were females. This is in similar most of the earlier case series from India which reported a higher proportion of women suffering from CVT than men, except a series of 110 angiographically proven CVT by Parikh et al., which had a male dominance. [5] A large hospital-based case series of 317 patients with CVT recruited over a period of 8½ years during the 80’s had only 15 male patients. [6] Nagaraja D et al stated that women are more exposed to predisposing factors like pregnancy and peripartum state and use of OCP.

Most of the patients were between the age group of 21-40 years. There were 23/50 [46%] in age group 21-30 years and 8 [16%] in 31-40 years. Thus the maximum

numbers of patients were in between 21-40 years [31/50 or 62%]. The oldest patient in this study was 72 years old. The youngest patient was 14 year old female. The mean age of the patients was 33.2. The mean age of patients in the large studies published from India ranged from 31.3 to 48.7 years. In the largest hospital-based prospective cohort study from India (Nizam's Institute Venous Stroke Registry [NIVSR]) by Narayan et al., 428 consecutive patients with CVT were enrolled over a period of 8 years from a tertiary care hospital from South India, the mean age of the patients in this study being 31.3 years. [7]

In CVST, large numbers of symptoms are associated with variable presentation. In contrast to the arterial stroke, which can be easily diagnosed clinically in a majority of the cases, CVT has no single pattern of presentation, and it may be difficult to diagnose it on clinical grounds alone. Clinical findings in CVT fall into two major categories: Those related to increased intracranial pressure due to impaired venous drainage; and, those related to focal brain injury from venous ischemia/infarction or hemorrhage. In this study, headache was the most common symptom in 48/50 patients (96%), followed by paresis in 23/50 patients (46%) and seizures in 22/50 patients (44%). Headache is the most frequent and most of the times, the earliest symptom of CVT. In the NIVSR cohort, 88.3% patients had headache as the presenting complaint with CVT.[7] The mechanism of headache is postulated to be the stretching of nerve fibers in the walls of the occluded sinus and local inflammation, as suggested by the evidence of contrast enhancement of the sinus wall surrounding the clot. Seizures are far more frequently seen in CVT than in arterial stroke with a frequency of 35–50% of all patients suffering from it, with an even higher incidence in peripartum CVT (76%). [8] The mental status may be quite variable, with patients showing no change in alertness, developing mild confusion or progressing to coma. Earlier case series from India

reported that 43% to 93% of patients had an altered sensorium at presentation. [9] In our study, altered mental status was found in 15/50 (30%), and seven patients (14%) presented with coma.

More than 100 putative causes of CVT have been described in the literature. The risk factors for venous thrombosis, in general, are linked classically to the Virchow triad of stasis of the blood, changes in the vessel wall, and changes in the composition of blood. Puerperium and pregnancy, as predisposing factors for CVT, are well known. Most of the pregnancy-related CVT occurs in the third trimester or puerperium. Pregnancy induces several prothrombotic changes in the coagulation system that persists at least during early puerperium. Most of the earlier case series of CVT reported from India have very high proportions of puerperal CVT. In 1984, Srinivasan, reported 135 cases of stroke in women, of whom only 6 had an arterial stroke, and the rest had a CVT. [10] In our study, pregnancy or puerperium was the risk factor in 52% of the patients. There is ample evidence to suggest a causal relationship between oral contraceptives (OCPs) and CVT. In a meta-analysis of 17 studies, summary odds ratio for developing cerebral venous sinus thrombosis (CVST) was 5.59 in women using OCPs compared with controls. In our study, 5 patients took OCPs for minimum period of 3 months before the development of CVST. The most common risk factor identified for CVT throughout the world is often a prothrombotic condition. In the ISCVT cohort, a prothrombotic condition was found in 34% of all patients, and a genetic prothrombotic condition was found in 22% of all patients. [11] In our study, genetic thrombophilia in 3/50 (6%), and acquired prothrombotic condition in 2 (4%) were identified. Protein C deficiency in 2 patients, Protein S deficiency in 1 patient, Nephrotic syndrome in 1 patient and Antiphospholipid antibody syndrome in 1 patient were the prothrombotic conditions identified in our study.

Although infective causes of CVST were frequently reported in the earlier series, they account for a very small percentage of patients in our study (10%). This could be due to the availability of potent broad spectrum antibiotics in today's era.

In our study, 20% of cases were idiopathic. Despite the continuous description of new causes, in about 13% of patients, no etiology can be found in the recent series also. [11] Therefore, the search for an etiology remains a difficult problem in CVST.

Cerebral venous thrombosis is multifactorial, and identification of one risk factor should not deter the clinician from searching for more causes. In our study, 8% of cases were multifactorial. Narayan et al. reported 18.2% patients having multiple risk factors in their study from South India. [7]

In most of the patients, multiple segments of dural venous sinuses were involved at a time. The involvements of deep venous and cortical veins are much less than venous sinuses. In our study about 92% of cases, dural venous sinuses were involved. Deep venous system was found affected in 12% of cases. These findings are similar to the findings of Bousser et al., who stated that thrombosis of deep cerebral venous system is rare and difficult to diagnose. [12] Commonest association was noticed between superior sagittal and transverse or sigmoid sinus. These findings are similar to the findings of Greiner et al. [13] They concluded that in veno-occlusive stroke, the superior sagittal sinus followed by transverse, sigmoid, and straight were generally involved.

In earlier studies, CVT was diagnosed mainly at autopsy and was considered to be lethal, with the mortality figures ranging from 30% to 50%. With the advent of newer imaging modalities and increased sensitization towards diagnosing CVT, the mortality rates have decreased. Death had occurred in 10 % of cases in this study. Poor prognostic factors at the time of admission were stupor or coma (P=0.001)

and parenchymal with or without subarachnoid hemorrhage in neuroimaging (P=0.005). Pai et al., reported an in-hospital mortality of 12.9% in their cohort of 612 patients. [14]

## CONCLUSION

Cerebral venous sinus thrombosis is a rare condition but commonly affecting young female of age group 21-30 years. Puerperium and pregnancy are the most common cause of cerebral venous sinus thrombosis in this study. Headache is present in almost all the patients with cerebral venous sinus thrombosis. MR venography in most of the patient thrombosis was suggestive of more than one sinus. Involvement of superior sagittal sinus is most common either alone or along with other sinuses. In this study, majority of patients had complete recovery on discharge with anticoagulant therapy. Death had occurred in 10% of cases. We conclude that the overall prognosis of CVST is fairly good, at least for independent survival. Coma and intracerebral haemorrhage are independent predictors for poor outcome.

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