

## Original Research Article

# Clinical features, predisposing factors and radiological study of cerebral venous sinus thrombosis: experience from a tertiary care center in Southern India

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**Received:** 18 April 2017

**Accepted:** 18 May 2017

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## ABSTRACT

**Background:** Cerebral venous thrombosis (CVT) is a less common cause of stroke with a wide range of clinical presentations, predisposing factors, radiological features and outcomes. A high index of suspicion is absolutely essential to diagnose cerebral venous thrombosis. In this article, we have reviewed the clinical spectrum and radiological profile of patients with cerebral venous thrombosis and attempted to identify the specific predisposing factors for developing cerebral venous thrombosis particularly in this region of India.

**Methods:** 116 patients hospitalized from January 2015 to March 2017 with a final diagnosis of Cerebral Venous Thrombosis which was confirmed by imaging (MRI/MRV or CT angiography) were included. Patients who were initially diagnosed as CVT but imaging were not suggestive of the same were excluded.

**Results:** The mean age of the study population was 35.21 years, with most patients aged between 21-30 years. 18.1% of the study population were puerperal women, much lower than earlier series. 54.54% of the men had a significant history of alcohol consumption and 10.34% of the non-puerperal women revealed a history of consuming oral contraceptive pills. Among men, seizures were the most common presenting symptom followed by headache. Women presented with headache followed by vomiting. Superior sagittal sinus, transverse sinus, cortical veins and sigmoid sinus involvement were quite common in comparison to the other sinuses.

**Conclusions:** Accurate and prompt diagnosis of CVT is crucial because timely and appropriate therapy can reverse the disease process and significantly reduce the risk of acute complications and long-term sequelae. In this article, we have reviewed the epidemiology, causative factors, clinical features and as well as radiological pattern of CVT from an Indian perspective. Over the last decade, a relatively high incidence of CVT in fairly young individuals warrants further evaluation towards genetic predisposition for pro-thrombotic states particularly in this region of India.

**Keywords:** Alcohol, CVT, Intracranial thrombosis, Neuroimaging

## INTRODUCTION

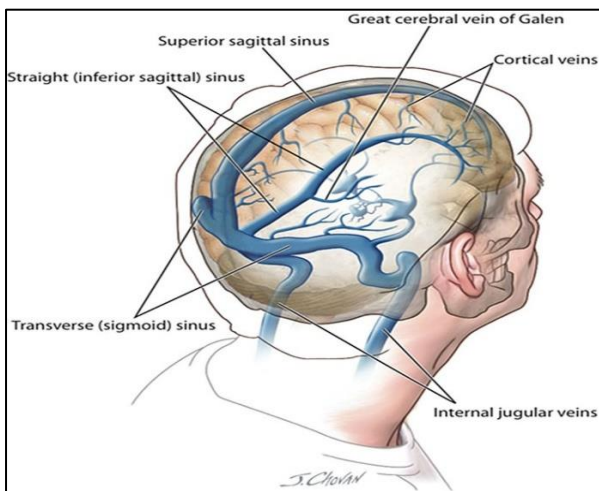
Cerebral venous thrombosis (CVT) is a less common cause of stroke with a wide range of clinical presentations, predisposing factors, radiological features and outcomes. The earliest known description of CVT

appeared in French literature back in 1825. The diagnosis was arrived at autopsy in a man who had suffered severe headaches and seizures for 6 months. For decades that followed, almost all cases were diagnosed at autopsy, until venography was introduced in the second half of the 20<sup>th</sup> century. As imaging modalities like Computed

Tomography (CT) and magnetic resonance venograms (MRV) became available, more cases are being diagnosed and treated than ever before.<sup>1,2</sup>

CVT may occur in any age group, a large number of reported cases were women in association with puerperium. This association was found to be 10-12 times more frequent in India than in Western countries. Most of the earlier case series from India reported a higher proportion of women suffering from CVT than men. Conversely, the recent case series do not show this trend of female dominance. One reason for this change may be attributed to improved obstetric care in the country.<sup>3-5</sup>

These patients present with severe headaches, features of raised intracranial tension, seizures, varying degrees of impaired consciousness, cranial nerves impairment, motor and sensory disturbances in the extremities. The underlying pathological mechanism of the disease is the impairment of venous outflow from the brain parenchymal tissue (Figure 1). An obstruction of a major drainage pathway leads to the development of venous intracranial hypertension, cerebral edema, and consequently, CSF hypertension (Figure 2). The ventricles of the brain usually stay at normal size, or become slit-like as a result of the surrounding edema. In the most severe cases, ischemia and/or haemorrhages may develop in the brain tissue.<sup>6,7</sup>

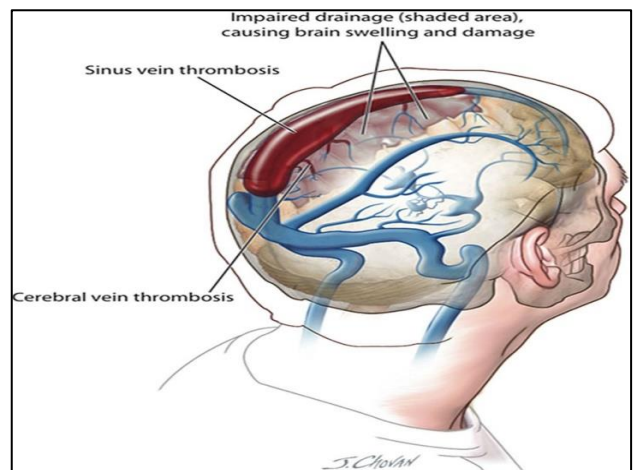


**Figure 1: The anatomy of the cerebral veins and sinuses.**

A high index of suspicion is absolutely essential to diagnose cerebral venous thrombosis. Diagnosis is basically clinical, but with the advent of CT and MR Venograms, the diagnosis of CVT has improved significantly. CT scan commonly shows haemorrhagic infarctions with or without “cord”, or “empty delta” sign. The most sensitive investigation modality to confirm the diagnosis is MRI in combination with magnetic resonance venography. T<sub>1</sub> and T<sub>2</sub>-weighted MRI may show a hyper intense signal from the thrombosed sinuses if recently formed.

The combination of an abnormal signal in a venous sinus and a corresponding absence of flow on magnetic resonance venography confirms the diagnosis of thrombosis.<sup>8</sup>

In the past, when CVT was diagnosed almost exclusively at autopsy, the disease was thought to be almost always fatal. In early angiographic series, mortality ranged between 30% and 50%. In more recent series, widely discrepant proportions of case fatality ranging from 4% to 33% were reported. In the International study on cerebral vein and dural sinus thrombosis (ISCVT) where 624 cases were studied, 4.3% of patients died during the acute phase of CVT and 3.4% within 30 days from symptom onset. Most deaths were due to trans-tentorial herniation, more so in the acute phase. The reduction in mortality could be attributed to the early diagnosis and prompt treatment with parenteral anticoagulants followed by oral agents.<sup>9</sup>



**Figure 2: Thrombosis of the superior sagittal sinus.**

More and more cases of CVT are now being diagnosed and important developments have been made in our understanding of the pathophysiology of it. Despite the advances, CVT remains a diagnostic challenge and is a potentially lethal disease. High index of suspicion and awareness of the clinical features and the predisposing factors with the aid of imaging techniques can help in the diagnosis of most cases. With improved diagnosis and prompt treatment, it is possible to achieve an exceptional outcome for most patients.<sup>8</sup>

The objective of this study was to study the clinical spectrum and radiological profile of patients with cerebral venous thrombosis. And identify the predisposing factors for developing cerebral venous thrombosis.

## METHODS

This study was performed as a hospital based retrospective and prospective observational study at SDM College of Medical Sciences hospital at Dharwad,

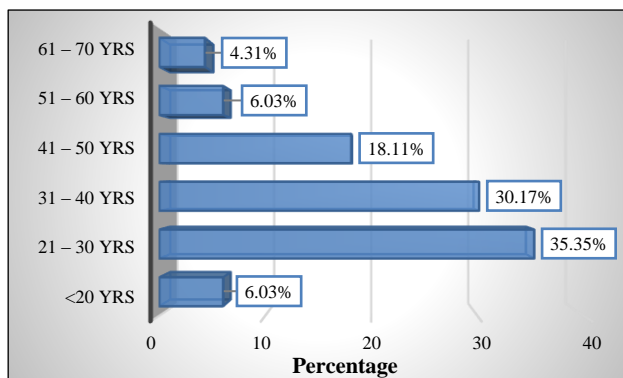
Karnataka, India. 116 patients hospitalized from January 2015 to March 2017 with a final diagnosis of Cerebral Venous Thrombosis which was confirmed by imaging (MRI/MRV or CT angiography) were included. Patients who were initially diagnosed as CVT but imaging were not suggestive of the same were excluded.

A Structured preformat was prepared and 116 patients were enrolled in the study. Detailed history with presenting complaints, onset of illness and predisposing factors were recorded. A thorough neurological examination was performed on each patient. The data regarding radiological investigations were retrieved through medical records.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS). Continuous variables were presented in titre of mean. Categorical variables were expressed as proportions and proportion percentages were calculated.

**RESULTS**

56.9% of the study population were men. The mean age of the study population was 35.21 years, with most patients aged between 21-30 years (Figure 3). 43.1% of the study population were women and 42% of the women (18.1% of the study population) were in the puerperal period (Figure 4). 39.65% of the patients presented within 48 hours of symptom onset; however, most patients (56.04%) had a subacute presentation (Table 1). The average period of puerperium was 12.5 days.

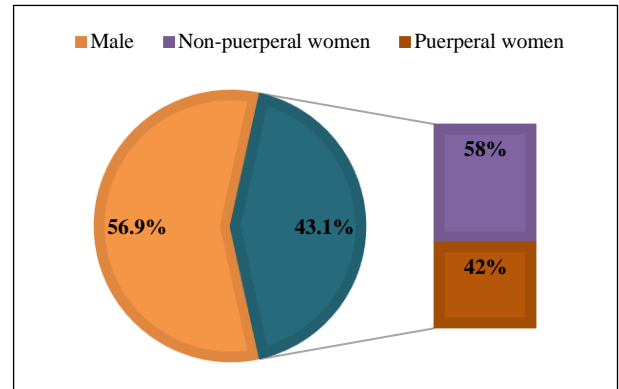


**Figure 3: Age distribution of patients.**

Among men, seizures were the most common presenting symptom followed by headache. Women presented with headache followed by vomiting. The relative occurrences of clinical symptoms varied among men and women (Figure 5). Cranial nerve impairment was observed in 8.62% of the patients while motor deficits were elicited in 20.68% (Table 1).

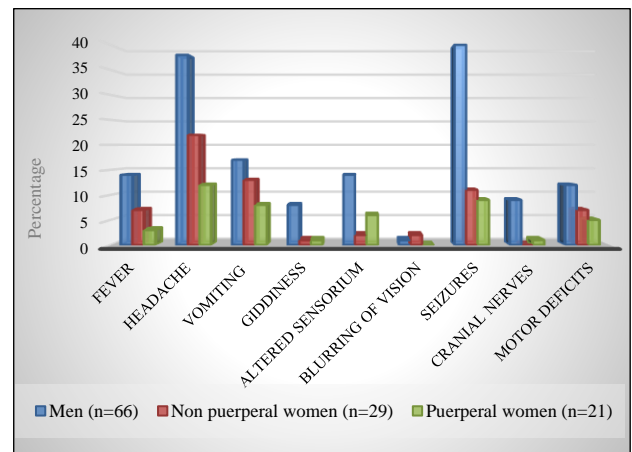
54.54% of the men had a significant history of alcohol consumption. 10.34% of the non-puerperal women revealed a history of consuming oral contraceptive pills. 1.72% of the population had a local infection in the form

of otitis and 2.58% had history of malignancy in the past. None of the patients had deep vein thrombosis in the past.

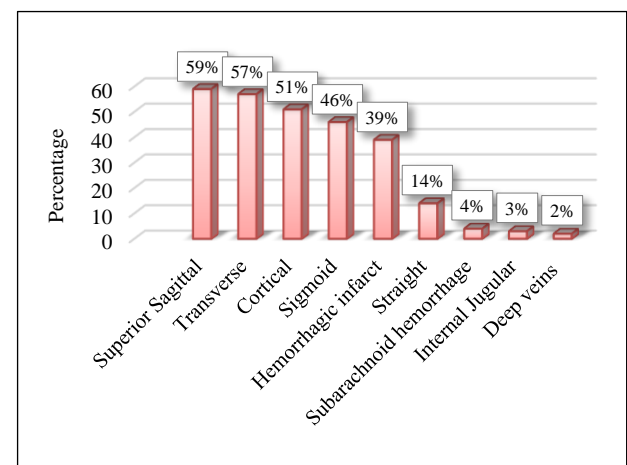


**Figure 4: Gender distribution of patients.**

Superior sagittal sinus, transverse sinus, cortical veins and sigmoid sinus involvement were quite common in comparison to the other sinuses. 39.62% of the patients suffered haemorrhagic infarcts, while 3.44% had evidences of subarachnoid hemorrhages (Figure 6).



**Figure 5: Relative occurrences of symptoms.**



**Figure 6: Radiological features of the patients studied.**

97 patients (83.6%) improved during the course in the hospital and were discharged; 16 patients (13.8%) left the hospital against medical advice. The mean duration of stay in the hospital was 8 days. 3 (2.58%) of the patients

studied expired 5 to 6 days after admission. All 3 patients were men and presented with seizures and altered mental status, consequently had superior sagittal sinus involvement and large haemorrhagic infarcts on imaging.

**Table 1: Clinical features, pathological factors and radiological pattern of involvement among patients.**

	Men (n=66)	Non-puerperal women (n=29)	Puerperal women (n=21)	Total (n=116)
<b>Clinical features</b>				
Fever	14 (21.21%)	7 (24.13%)	3 (14.28%)	24 (20.68%)
Headache	38 (57.57%)	22 (75.86%)	12 (57.14%)	72 (62.06%)
Vomiting	17 (25.75%)	13 (44.82%)	8 (38.09%)	38 (32.75%)
Giddiness	8 (12.12%)	1 (3.44%)	1 (4.76%)	10 (8.62%)
Altered sensorium	14 (21.21%)	2 (6.89%)	6 (28.57%)	22 (18.96%)
Blurring of vision	1 (1.51%)	2 (6.89%)	0	3 (2.58%)
Seizures	40 (60.6%)	11 (37.93%)	9 (42.85%)	60 (51.72%)
Cranial nerves	9 (13.63%)	0	1 (4.76%)	10 (8.62%)
Motor deficits	12 (18.18%)	7 (24.13%)	5 (23.8%)	24 (20.68%)
<b>Onset</b>				
Acute (<48h)	29 (43.93%)	4 (13.79%)	13 (61.9%)	46 (39.65%)
Subacute (48h-30d)	34 (51.51%)	24 (82.75%)	7 (33.33%)	65 (56.03%)
Chronic (>30d)	3 (4.5%)	1 (3.44%)	1 (4.76%)	5 (4.31%)
<b>Predisposing factors</b>				
Alcohol	36 (54.54%)	0	0	36 (31.03%)
Hormone therapy	-	3 (10.34%)	0	3 (2.58%)
Ear infection	2 (3%)	0	0	2 (1.72%)
Malignancy	0	3 (10.34%)	0	3 (2.58%)
<b>Radiological features</b>				
Superior Sagittal sinus	39 (59.09%)	11 (37.93%)	9 (42.85%)	59 (50.86%)
Transverse sinus	32 (48.48%)	15 (51.72%)	10 (47.61%)	57 (49.13%)
Sigmoid sinus	25 (37.87%)	13 (44.82%)	8 (38.09%)	46 (39.65%)
Deep veins	1 (1.51%)	0	1 (4.76%)	2 (1.72%)
Cortical veins	29 (43.93%)	15 (51.72%)	7 (33.33%)	51 (43.96%)
Straight sinus	8 (12.12%)	3 (10.34%)	3 (14.28%)	14 (12.06%)
Internal jugular vein	1 (1.51%)	2 (6.89%)	0	3 (2.58%)
Hemorrhagic infarct	21 (31.81%)	9 (31.03%)	9 (42.85%)	39 (33.62%)
SAH	1 (1.51%)	1 (3.44%)	2 (9.52%)	4 (3.44%)
Mortality	3 (4.5%)	0	0	3 (2.58%)

## DISCUSSION

Most of the earlier case series from India reported a higher proportion of women suffering from CVT in comparison to men, albeit for a few such as one done by Parikh et. al where 110 confirmed CVT cases which had a male dominance. This gender bias was attributed to gender-specific risk factors like the usage of oral contraceptives, pregnancy, puerperium, and hormone replacement therapy. In contrast to this, the recent case series from India do not show this trend of female dominance, including this study where 56.9% of the study population were men. The plausible reason for this variation in gender trends over the last two decades could be the improvement in obstetric care.<sup>5,10</sup>

In one of the largest hospital-based prospective studies from India 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 that study was 31.3 years. In comparison, the mean age of our study population was 35.21 years.<sup>11</sup>

Puerperium and pregnancy, as predisposing factors for CVT are well established. Most of the pregnancy-related CVT occurs in puerperium. As mentioned earlier, most of the earlier case series reported from India had very high proportions of puerperal CVT. In recent times, a change in this trend has been noted including the findings in our study. Only 18.1% of the study population were puerperal women, compared to the NIVSR cohort study and the



study by Pai et al where there were 9.8% and 8% pregnancy related CVT cases respectively.<sup>11,12</sup>

In the west, oral contraceptives (OC) as a risk factor for CVT has been more frequently reported compared to countries like India. In the prospective International study on cerebral vein and dural sinus thrombosis (ISCVT) cohort of 624 adults with CVT, 46% of women who developed CVT were on OC's, which made it the third most important risk factor. In India, almost all the large series have shown a much lower proportion of OC usage as a risk factor for CVT compared to those from the west. One such example was the NIVSR study where 11.4% patients had usage of OCs. In our study, that proportion was even lower with only 6% revealing the usage of OCs. This can be attributed to the variations in the socio-economic environment in India compared to the western nations where the usage and acceptance of OCs are significantly higher.<sup>9,11</sup>

The association of alcohol consumption and the occurrence of CVT has not been well established. However, in our study, 54.54% of the men had significant consumption of alcohol. One other study from South India conducted by Rathi M et al showed a similar picture, where alcohol was etiologically related in 45.45% of cases. Some studies point towards dehydration and resultant hyper viscosity of blood induced by heavy alcohol consumption as a possible predisposition for thrombosis, although the mechanisms of which are yet unclear.<sup>13,14</sup>

Headache is the most common and usually, the earliest symptom of CVT. The incidence of headache in other studies range between 75-88% In our study, headache was the commonest symptom, occurring in about 62% of the patients. Seizures, particularly generalized tonic-clonic seizures occurred in 51.72% of the patients. Seizures occur far more frequently in CVT than in arterial strokes, ranging between 35-50%. Seizures were much more common in men (60%) than in women in our study. The mental status may be quite inconstant, with patients showing no change in alertness, developing mild confusion or presenting with coma. Recent studies show a lower proportion of patients (25%) having changes in sensorium at presentation compared to those from the past. In our study, only 19% of the patients presented with an altered mental state. The reason for this reduction is probably due to patients seeking medical help earlier in the recent times.<sup>9,11,15</sup>

The superior sagittal sinus was most common sinus involved in just over 50% of the cases, usually with other sinuses. In studies by Ameri et al and Daif et al, superior sagittal sinus was involved in 72% and 85% of patients respectively. Other sinuses involved in decreasing order of frequency were the transverse sinuses, cortical veins and sigmoid sinus (Figure 6).<sup>15,16</sup>

In hospital mortality of CVT patients ranges between 7.7% and 12.9% in large series. However, in our study, 2.58% of the patients studied expired. Although 13.8% of the patients left against medical advice and their outcome could not be determined.<sup>11,12</sup>

## CONCLUSION

CVT is an important and treatable cause of stroke affecting men more than women in this region of India. Headache followed by seizures are the common presenting features. The most significant risk factor was alcoholism especially in young men with CVT, while conventional risk factors like postpartum state are reducing in frequency. The relatively high incidence of CVT in fairly young individuals warrants further evaluation towards genetic predisposition for pro-thrombotic states in this region of India.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Aneesh T, Gururaj H, Arpitha JS, Rao A, Chakravarthy V, Shetty A. Clinical features, predisposing factors and radiological study of cerebral venous sinus thrombosis: experience from a tertiary care center in Southern India. *Int J Res Med Sci* 2017;5:3023-8.