

STUDY ON ETIOLOGY, CLINICAL PROFILE AND MANAGEMENT OF CEREBRAL VENOUS THROMBOSIS

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ABSTRACT

Background: Cerebral venous thrombosis (CVT) is an uncommon cerebrovascular disorder with variable clinical manifestations and diverse thrombotic risk factors. The aim is to evaluate the clinical profile, etiological and thrombotic risk factors, laboratory abnormalities, venous sinus involvement, and neuroimaging findings among patients diagnosed with cerebral venous thrombosis. **Materials and Methods:** This observational study was conducted at SRM Medical College Hospital and Research Centre, Kanchipuram district, among patients admitted with CVT between February 2014 and January 2016. Sixty patients with imaging-confirmed CVT were included. Clinical manifestations, lifestyle-related risk factors, serum homocysteine, thrombophilia-related laboratory findings, and venous sinus involvement on CT, MRI, and/or MR venography were recorded. Clinical outcome was assessed according to neurological status during follow-up or at the end of treatment. Categorical variables were analysed using the Pearson chi-square test, with $p < 0.05$ considered statistically significant. **Result:** Among 60 patients, 39 (65%) were male and 21 (35%) were female. The 21–25-year age group was most frequent (23.3%), followed by 31–35 years (20.0%). Smoking was reported in 60% and alcohol use in 82%. Headache was present in all patients, followed by seizures (80%) and vomiting (65%). Elevated serum homocysteine was the most frequent laboratory abnormality (58.3%). Antinuclear antibodies were positive in 16.7%, protein C deficiency in 8.3%, protein S abnormality and anticardiolipin antibodies in 5% each, and antithrombin III abnormality in 3.3%. Superior sagittal sinus involvement was most frequent (71.7%), followed by transverse sinus involvement (43.3%). Complete clinical improvement occurred in 86.7%, while 13.3% had residual neurological deficits. **Conclusion:** CVT showed variable clinical and laboratory profiles, with headache being the predominant presentation, hyperhomocysteinemia the most frequent laboratory abnormality, and superior sagittal sinus the most commonly involved venous sinus.

INTRODUCTION

Cerebral venous thrombosis (CVT) is an uncommon but a clinically important cerebrovascular disorder which was caused by a thrombus in the cerebral veins or dural venous sinuses. The obstruction of venous drainage can increase intracranial pressure and results in cerebral oedema, venous infarction, or intracranial haemorrhage. CVT can occur across a wide age range in young adults and women with childbearing age. Its development is due to more than one factor, including hormonal changes, infections, inflammatory conditions, and inherited or acquired prothrombotic states.^[1-3] The clinical effects of CVT depend on where the thrombosis occurs and how extensive it is. Impaired venous drainage can increase

venous pressure and cause congestion, edema, ischemic injury, and hemorrhage. Patients may therefore present with headache, seizures, focal neurological deficits, altered consciousness, or encephalopathy. Since the symptoms can vary with the site of venous involvement, CVT may be difficult to recognize, in patients who do not have the more unique clinical features.^[1,4]

The epidemiological pattern of CVT also differs from that of conventional arterial stroke. It affects younger individuals, with hormonal and sex-related factors which plays an important role. Pregnancy, the puerperium, and exposure to exogenous estrogen are linked to women of reproductive age.^[5-7] Pregnancy and the puerperium are important because changes in coagulation and venous circulation can increase

thrombotic susceptibility. Although improvements in diagnosis and treatment have resulted better outcomes, some patients may still develop neurological, cognitive, or neuropsychiatric problems after CVT.^[8] The risk factors for CVT include both temporary and persistent prothrombotic conditions. Pregnancy, puerperium, estrogen-containing oral contraceptives, infections, inflammatory disorders, malignancy, trauma, and surgery may increase thrombotic risk through changes in coagulation, inflammation, endothelial injury, or venous stasis.^[9,10]

Inherited thrombophilias, such as factor V Leiden and prothrombin gene variants, as well as deficiencies of protein C, protein S, and antithrombin, can also increase susceptibility. Acquired conditions, including antiphospholipid antibodies and hyperhomocysteinemia, are additional contributors.^[9-11] These factors may occur separately or together, and in some patients the cause remains difficult to establish. Even after detailed evaluation, patients have no clearly identifiable risk factor. These apparently idiopathic cases explain the complex nature of CVT and highlight the importance of a systematic assessment of possible risk factors. Identifying such factors can assist with etiological classification and may also guide decisions about further thrombophilia evaluation.^[8-10]

Diagnosis remains challenging because CVT can present with nonspecific symptoms, particularly headache, and may occur without obvious neurological deficits. The clinical presentation, associated thrombotic risk factors, laboratory abnormalities, venous sinus involvement, and imaging findings may vary considerably between patients. A systematic assessment of these features is therefore important for better characterization of the disease and for identifying underlying thrombotic risk factors.

Aim

This study aimed to evaluate the clinical profile, etiological and thrombotic risk factors, laboratory abnormalities, venous sinus involvement, and neuroimaging findings among patients diagnosed with cerebral venous thrombosis.

MATERIALS AND METHODS

This observational study was conducted at SRM Medical College Hospital and Research Centre, Kanchipuram district. Patients admitted with CVT between February 2014 and January 2016 were included in the study.

Inclusion and Exclusion criteria

The study included adult patients with clinical features suggestive of cerebral venous thrombosis and imaging confirmation of the diagnosis. The original study methodology specified an age range of 15-70 years. Patients with bleeding diathesis, neoplastic disease, evidence of central nervous

system infection, or imaging evidence of arterial infarction were excluded.

Methods: A total of 60 patients diagnosed with CVT were included. The study population comprised both male and female patients admitted with acute headache and other neurological manifestations suggestive of CVT. The diagnosis was confirmed by CT, MRI, and/or MR venography according to the available imaging findings. All patients underwent detailed history taking to identify potential risk factors for CVT. General and neurological examinations were performed, with particular attention to papilloedema, seizures, focal neurological deficits, and other presenting neurological features. Smoking and alcohol use were also recorded as potential risk factors. Laboratory investigations included serum homocysteine and thrombophilia-related tests. These included antinuclear antibodies, lupus anticoagulant, anticardiolipin antibodies, protein C, protein S, and antithrombin III. The findings were recorded according to the available laboratory results.

Neuroimaging was performed for confirmation and assessment of the extent of CVT. CT, MRI, and MR venography findings were evaluated for venous sinus involvement. The recorded sites included the superior sagittal sinus, transverse sinus, sigmoid sinus, straight sinus, and deep cerebral veins. Associated findings such as haemorrhage were also documented where present. Clinical outcome was assessed according to the neurological status documented during follow-up or at the end of the treatment period.

Statistical analysis: Data were presented as mean, frequency, and percentage. Continuous variables were summarized using mean values. Categorical variables were compared using the Pearson chi-square test. Significance was defined by a p-value less than 0.05 using a two-tailed test. Data analysis was performed using SPSS version 17.0.

RESULTS

Among the 60 patients (39 male and 21 female), the 21-25 years age group was the most common, with 14 (23.3%) patients, followed by 31-35 years with 12 (20.0%). Both the 26-30- and 41-45-years groups included 10 (16.7%) patients. The 36-40- and 46-50-years groups accounted for 7 (11.7%) and 6 (10.0%) patients, respectively. The <20, 51-55, 56-60, and >60 years groups each had 1 (1.7%) patient. Smoking was reported in 36 (60.0%) patients and was absent in 24 (40.0%). Similarly, alcohol use was present in 49 (82%) patients [Table 1].

Headache was present in all 60 (100%) patients. Seizures were reported in 48 (80%), followed by vomiting in 39 (65%). Focal motor deficit/hemiparesis was seen in 28 (46.7%) patients, papilloedema in 24 (40%), diplopia in 22 (36.7%), and aphasia in 8 (13.3%). The corresponding absent findings were 0 (0%), 12 (20%), 21 (35%), 32

(53.3%), 36 (60%), 38 (63.3%), and 52 (86.7%), respectively [Table 2].

Table 1: Age distribution and selected lifestyle-related risk factors among patients with cerebral venous thrombosis

		N (%)
Age (in years)	<20	1 (1.7%)
	21-25	14 (23.3%)
	26-30	10 (16.7%)
	31-35	12 (20%)
	36-40	7 (11.7%)
	41-45	10 (16.7%)
	46-50	6 (10%)
	51-55	1 (1.7%)
	56-60	1 (1.7%)
	>60	1 (1.7%)
Smoking	Present	36 (60%)
	Absent	24 (40%)
Alcohol use	Present	49 (82%)
	Absent	11 (18%)

Table 2: Clinical manifestations among patients with cerebral venous thrombosis

		N (%)	
		Present	Absent
Clinical Manifestation	Headache	60 (100%)	0
	Vomiting	39 (65%)	21 (35%)
	Seizures	48 (80%)	12 (20%)
	Diplopia	22 (36.7%)	38 (63.3%)
	Papilloedema	24 (40%)	36 (60%)
	Focal motor deficit/hemiparesis	28 (46.7%)	32 (53.3%)
	Aphasia	8 (13.3%)	52 (86.7%)

Among the laboratory findings, higher serum homocysteine was the common abnormality, observed in 35 (58.3%) patients, while 25 (41.7%) had normal levels. Antinuclear antibodies were positive in 10 (16.7%) patients and negative in 50 (83.3%). Protein C deficiency was reported in 5 (8.3%) patients, whereas 55 (91.7%) had negative findings. Anticardiolipin antibodies and protein S

abnormalities were each observed in 3 (5%) patients, with negative findings in 57 (95%) patients for each test. Antithrombin III abnormality was present in 2 (3.3%) patients, while 58 (96.7%) had negative findings. Lupus anticoagulant was the less common abnormality, reported in 1 (1.7%) patient, but 59 (98.3%) had negative findings [Table 3].

Table 3: Distribution of thrombophilia-related laboratory findings among patients with cerebral venous thrombosis

	N (%)	
	Positive/elevated	Negative/normal
Serum homocysteine	35 (58.3%)	25 (41.7%)
Antinuclear antibodies (ANA)	10 (16.7%)	50 (83.3%)
Lupus anticoagulant (LA)	1 (1.7%)	59 (98.3%)
Anticardiolipin antibodies	3 (5%)	57 (95%)
Protein C	5 (8.3%)	55 (91.7%)
Protein S	3 (5%)	57 (95%)
Antithrombin III	2 (3.3%)	58 (96.7%)

Elevated serum homocysteine was found in 32 (65%) patients with alcohol use and 3 (27%) without alcohol use. Normal levels were seen in 17 (35%) and 8

(73%) patients, respectively, with a significant association ($p=0.021$) [Table 4].

Table 4: Association between alcohol consumption and serum homocysteine levels among patients with cerebral venous thrombosis

		Serum homocysteine level N (%)		P Value
		Elevated	Normal	
Alcohol consumption	Absent	3 (27%)	8 (73%)	0.021
	Present	32 (65%)	17 (35%)	

Superior sagittal sinus involvement was the most frequently observed venous sinus abnormality, occurring in 43 (71.7%) patients, followed by transverse sinus involvement in 26 (43.3%) patients. Straight sinus involvement was observed in 18 (30%)

patients, while sigmoid sinus involvement was present in 16 (26.7%) patients. Deep cerebral vein involvement was identified in 9 (15%) patients, whereas cavernous sinus involvement was the least frequent, occurring in 2 (3.3%) patients. Eight

patients had residual neurological deficit including Aphasia, Hemiparesis. The rest of the patients improved totally [Table 5].

Table 5: Distribution of cerebral venous sinus involvement among patients with cerebral venous thrombosis

		N (%)
Cerebral venous sinus involved	Superior sagittal sinus (SSS)	43 (71.7%)
	Transverse sinus (TS)	26 (43.3%)
	Sigmoid sinus (SG)	16 (26.7%)
	Straight sinus (HE)	18 (30%)
	Deep cerebral veins (DEEP)	9 (15%)
	Cavernous sinus (CAV)	2 (3.3%)
Outcome	Residual neurological deficit	8 (13.3%)
	Complete improvement	52 (86.7%)

Among 43 patients with SSS involvement, SSS alone was seen in 28 (65.1%), SSS + TS in 13 (30.2%), and SSS + HE in 11 (25.6%). The remaining patterns ranged from 6 (14.0%) to 1 (2.3%). Among 26 patients with TS involvement, TS + SSS occurred in

13 (50.0%), TS + SSS + SG in 15 (57.7%) each, and TS alone in 4 (15.4%). Deep CVT was associated with SSS in 8 (88.9%) and TS in 1 (11.1%) patient [Table 6].

Table 6: Pattern of superior sagittal, transverse and deep cerebral venous sinus involvement among patients with cerebral venous thrombosis

		N (%)
Superior sagittal sinus (SSS) involvement	SSS involvement alone	28 (65.1%)
	SSS + TS	13 (30.2%)
	SSS + SG	1 (2.3%)
	SSS + TS + SG	6 (14%)
	SSS + TS + SG + HE	2 (4.7%)
	SSS + TS + HE	1 (2.3%)
	SSS + HE	11 (25.6%)
	SSS + DEEP	4 (9.3%)
	SSS + SAH	4 (9.3%)
Transverse sinus (TS) involvement	TS alone	4 (15.4%)
	TS + SG	9 (34.6%)
	TS + SSS + SG	15 (57.7%)
	TS + SSS	13 (50%)
	TS with all sinuses	26 (100%)
	TS + SG + haemorrhage	2 (7.7%)
	Isolated TS + haemorrhage	2 (7.7%)
Deep cerebral venous thrombosis	Deep CVT with associated SSS thrombosis	8 (88.9%)
	Deep CVT with associated TS involvement	1 (11.1%)

DISCUSSION

In our study, CVT was seen mainly in younger adults, with the highest number of patients in the 21-25-year group, followed by the 31-35-year group. Tak et al. reported a mean age of 34.29 years, with most patients aged 25-35 years, while Thammishetti et al. reported a mean age of 29.5 ± 9.68 years.^[12,13] Kasiviswanathan et al. found that 44.3% of patients were aged 21-40 years.¹⁴ Dave et al. reported a mean age of 35 years, and Mamatarani et al. reported 35.9 years.^{15,16} These findings show a similar pattern of CVT occurring mainly among younger adults, although differences in age grouping and study characteristics may explain some variation.

In our study, smoking and alcohol use were frequently reported. Kasiviswanathan et al. reported alcohol use in 27.1% and smoking in 21.4% of patients.^[14] Murugaiyan et al. reported alcohol use in 52.7%, while Colaco et al. reported alcohol dependency in 36% of a 50-patient cohort.^[17,18] The differences between these studies may be related to

differences in patient characteristics and study selection.

In our study, headache was the most common clinical manifestation, followed by seizures and vomiting. Tak et al. reported headache in 95.1%, Thammishetti et al. in 96.25%, Murugaiyan et al. in 94.54%, and Mamatarani et al. in 80% of patients.^[12,13,16,17] Seizures were reported in 63.75% by Thammishetti et al, 67.2% by Murugaiyan et al., 60% by Mamatarani et al., and 28% by Colaco et al.^[13,16-18] Papilloedema was reported in 67.5%, 60%, and 98% by Thammishetti et al., Mamatarani et al., and Colaco et al., respectively.^[13,16,18] Mamatarani et al. also reported vomiting in 30%, focal deficits in 50%, double vision in 7.5%, and dysphasia in 10%.^[16] These differences may be related to variations in clinical presentation, referral patterns, examination methods, and patient characteristics.

In our study, alcohol use was significantly associated with serum homocysteine levels. Kasiviswanathan et al. reported hyperhomocysteinemia in 40% of patients, while Dave et al. reported elevated homocysteine in 25%.^[14,15] Kamran et al. studied 76

patients with CVT using fasting assays and also reported significantly elevated homocysteine levels.¹⁹ Differences in laboratory methods, reference thresholds, nutritional status, and patient characteristics may explain the variation in homocysteine findings.

In our study, the superior sagittal sinus was frequently involved, either alone or together with other sinuses. Tak et al. reported SSS involvement in 38.1%, Kasiviswanathan et al. in 51.4%, and Mamatarani et al. in 62.5% of patients.^[12,14,16] Mamatarani et al. also reported TS involvement in 52.5%. Murugaiyan et al. reported SSS involvement in 34.5% and TS involvement in 20%.^[16,17] Dave et al. identified the transverse and sigmoid sinuses as the most commonly involved sites, although numerical proportions were not provided.^[15] Differences may be related to thrombus distribution, patient characteristics, imaging methods, and the way combined sinus involvement was recorded.

In our study, most patients showed clinical improvement, although some had residual neurological deficits. Kasiviswanathan et al. reported complete recovery in 93% of patients, with residual deficits in five patients.^[14] Santana et al. reported 3 deaths (7.6%) among 39 admissions, with focal deficits in 31%.^[20] Differences in follow-up duration, disease severity, patient selection, and outcome definitions may account for the variation between studies. These findings highlight the importance of consistent follow-up and standardized assessment of neurological outcome in patients with CVT.

CONCLUSION

In this study, hyperhomocysteinemia was the most common laboratory abnormality, while superior sagittal sinus involvement was the most frequent venous sinus finding. Headache, focal neurological deficits, seizures, vomiting and papilloedema were among the clinical presentations observed. Neuroimaging was important for confirming the diagnosis and showing the site and extent of venous involvement. Since CVT may present with nonspecific symptoms, early diagnosis can be difficult. Careful assessment of thrombotic risk factors together with appropriate imaging may help in making the diagnosis and starting treatment early. Thus, early recognition, timely treatment, and assessment of underlying prothrombotic conditions are important for better outcomes and appropriate preventive care.

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