

Original Research Article

Clinical presentation, risk factors and factors affecting short term outcome in patients with cerebral venous thrombosis

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ABSTRACT

Background: Cerebral venous thrombosis is a rare cause of stroke, with a predilection to females. Since the past two decades its morbidity and mortality had decreased because of the new effective diagnostic and therapeutic interventions. This study mainly intends to assess, the clinical and aetiological factors of cerebral venous thrombosis and the factors predicting its short-term outcome. Objective was to study the factors influencing the short-term outcome of CVT and to study the pattern of clinical presentation and risk factors for CVT.

Methods: It was a cross-sectional study done at a tertiary care Centre in Tamil Nadu, in adult CVT patients from August 2018 to August 2019. Clinical, aetiological and radiological data were collected from patients and assessed and factors influencing the short-term outcome at discharge and at 15 days after discharge were studied. Data was analysed using SPSS16 software. Analysis of the descriptive data was performed and independent factors influencing the short-term outcome were analysed subsequently.

Results: Males predominated in the study with a mean age of 38yrs. Most common presentation was headache. Infarct was present in 61 (56.5%). The most common site of venous involvement was superior sagittal sinus 81 (75%). Short term outcome had shown a significant association with hypertension (p value -0.019 and odds ratio- 65.439) and baseline MRS (p value- 0.000, OR - 0.004) only.

Conclusions: Nowadays, the mortality and morbidity of CVT has decreased. Hypertension has emerged as an independent predictive factor in the short-term outcome of CVT.

Keywords: Clinical presentation, Cerebral venous thrombosis, Patients, Risk factors, Short term outcome

INTRODUCTION

Ever since CVT was recognized in 19th century it remains as a diagnostic and therapeutic challenge.¹ Although very rare compared to arterial stroke it can occur at any age and usually occurs in young people and especially among women at puerperium.¹⁻³ The most common cerebral venous sinus affected in CVT is superior sagittal sinus followed by lateral sinus and in many of the cases more than one sinuses are also involved.^{1,3,4} It can have either acute, subacute or chronic

mode of presentation and its most serious consequence is the cerebral infarction, most commonly haemorrhagic infarction. Because of the recent diagnostic and therapeutic modalities, the morbidity and mortality rate of CVT has come down from 30-50% in the earlier days to less than 15%.^{1,2,4}

Compared to European studies, studies done in Asia show a difference in the aetiological spectrum of the disease probably due to geographical and cultural variation. According to most of the studies done in

Europe and other regions of the world most important causes of CVT included use of oral contraceptives, pregnancy and puerperium in females and alcoholism in males. Many other risk factors other than these conventional risk factors also contribute to CVT. They include dehydration, procoagulant state, infection, trauma, diabetes mellitus, connective tissue disorders, malignancies, anaemia, hypertriglyceridemia.^{1,2,4-7}

Manifestations of CVT can have a wide range, varying from nonspecific features of raised intracranial tension with or without focal neurological deficits and coma or altered sensorium. Usual symptoms of raised intracranial tension include head ache, papilledema and vomiting and the focal neurologic deficits usually present as aphasia, visual loss, diplopia, seizures, and cranial nerve palsy.⁷⁻⁹ Before the advent of the newer diagnostic modalities CVT was usually diagnosed on autopsy and so it was considered as a fatal disease but with the arrival of CT and MRI the outcome of CVT had become increasingly favorable. In some studies it was stated that if the patient successfully tide over the acute phase of CVT they will usually have a complete and rapid recovery.^{1,7,9,10}

Due to the wide range of clinical presentation and risk factors, which can even vary with different geographic regions, a very high index of suspicion is required for the diagnosis of CVT. In this study we are assessing the various clinical features, risk factors and the factors that affect the short-term outcome of patients with CVT in this Southern part of India.

Objectives was to study the factors influencing the outcome of CVT and to study the pattern of clinical presentation and risk factors for CVT.

METHODS

This is a Descriptive cross-sectional study. Conducted at Tertiary care Centre - PSG Institute of medical science, Peelamedu, Coimbatore, Tamil Nadu, South India for the Study period of one year from 2018 August to 2019 August.

Study Population includes Cerebral Venous Thrombosis patients visiting Neurology /Medicine Department as Outpatient or as inpatients. Sample size involves all patients visiting Neurology OPD or as inpatients in Department of Neurology / Medicine from 2018 August to 2019 August.

Inclusion criteria

All adult patients presented with features of cerebral venous thrombosis confirmed by CT/MRI brain and MR venogram.

Exclusion criteria

Patient less than 18 years.

Study had written consent from the patient and approval of Institutional Review Board. Baseline details were collected regarding the name, age, time of hospital admission from the onset of symptoms, mode of onset and duration of hospital stay. Detailed history and clinical examination of the patients were done to obtain the following details. Symptoms and signs - presence of headache, visual loss, diplopia, aphasia, history of seizures, either focal or generalised tonic clonic were taken. Patients were checked for signs such as papilledema, stupor/coma, left/right hemiplegia, cranial nerve palsy and anisocoria. Glasgow coma scale score was also noted. Patients were asked for a past history of diabetes mellitus, hypertension, coronary artery disease, dyslipidaemia, deep vein thrombosis, connective tissue disorders, thyroid disorders and any malignancy. Personal habits such as alcohol intake and smoking and drug history such as use of OCP, steroids and chemotherapy were also looked into.

Routine and other detailed investigational work up were done and a haemoglobin of less than 10gm% is taken as anaemia. Level of Hb was divided into 3 categories, 10gm%, 7-10gm% and, 7gm%. Total count of more than 11000/mm³ was considered as leucocytosis. ESR, PT, INR, blood sugar, blood urea, S.creatinine, lipid profile, electrolyte levels, HIV status, connective tissue profile such as ANA, Ds DNA and APLA, procoagulant work up for S.Homocysteine, S.Fibrinogen, Factor v laiden mutation, Protein C and S, Anti thrombin 3 levels and TSH levels were checked. X Ray PNS was taken to rule out sinusitis. Radiological features such as presence of infarct - Haemorrhagic or thrombotic, and site of venous thrombosis like, sigmoid sinus - right / left, superior sagittal sinus, transverse sinus right / left, straight sinus, deep venous system, cortical vein and jugular vein involvement were checked. Patients were assessed with a Modified Rankin Score (Appendix 1). Patients were divided based on Baseline MRS as less than or equal to 2 and more than 2. Good outcome at discharge and after 15 days was considered as an MRS of 0 and 1-6 was considered as bad outcome.

Statistical analysis

Statistical analysis was done using SPSS 16 software. Frequency and percentage of all factors were assessed using descriptive statistics. Univariate logistic regression was performed to assess the significance of each clinical and other risk factors and the independent factor predicting the outcome was assessed using multivariate logistic regression and a p value of less than 0.05 was considered as significant.

RESULTS

108 confirmed cases of CVT came during the study period of which the males predominated (69, 63.9%). The age of the cases ranged from 15-61yrs with a mean age of 38.5 yrs. (S.D-11.474) .Time since the onset of symptoms

to hospital admission varied from 1-60 days with a mean of 6.18 days (S.D - 8.098). Duration of hospital stay ranged from 2 to 21 days with a mean of 6.81 days (S.D-2.987), 96 (88.9%) had acute onset of symptoms whereas 8 (7.4%) had subacute and 4 (3.7%) had chronic onset.

Clinical presentation

Most common clinical presentation was headache (98,90.7%) followed by Focal neurological deficits (61,56.5%). Range of clinical presentations with their frequency and percentage was listed in Table 1.

Table 1: Clinical presentations with its frequency and percentage.

Clinical presentation	Frequency		Percentage	
	Present	Absent	Present	Absent
Headache	98	10	90.7	9.3
Papilledema	26	82	24.1	75.9
Stupor or coma	1	107	0.9	99.1
Anisocoria	1	107	0.9	99.1
Focal neurological deficits	61	47	56.5	43.5
Visual loss	4	104	3.7	96.3
Diplopia	20	88	18.5	81.5
Aphasia	9	99	8.3	91.7
Seizures	44	64	40.7	59.3
Focal seizures	11	97	10.2	89.8
GTCS	36	72	33.3	66.7
Left hemiplegia /hemiparesis	16	92	14.8	85.2
Right hemiplegia / hemiparesis	14	94	13	87
Cranial nerve palsy	15	93	13.9	86.1

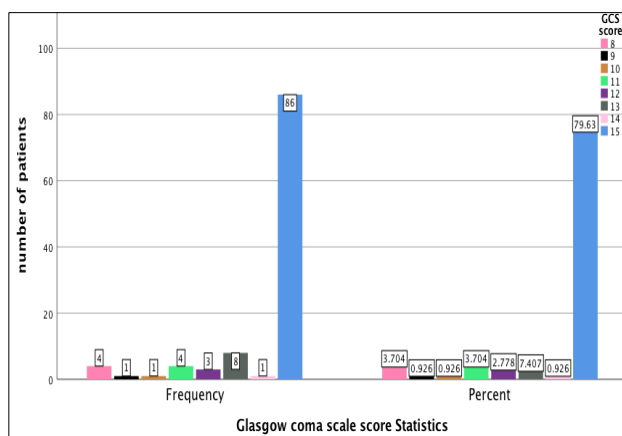


Figure 1: Glasgow coma scale Score of the patients with its frequency and percentage.

Glasgow coma scale

Glasgow coma scale score ranged from 8 to 15. Most of the patient's had a score of 15(86, 79.6%) and only few (5,4.6%) had got a GCS score less than 10 and those with GCS score between 10-15 were 17(15.7%). Glasgow coma scale score of each patient with its frequency and percentage is shown in figure 1.

Presence of comorbidities

Comorbidities were present in 59 (54.5%) and included dyslipidemia (26,24.1%), hypertension (23,21.3%), diabetes mellitus (19,17.6%), Coronary artery disease (3,2.8%), DVT (4,3.7%), connective tissue disorder (18,16.7%), thyroid disorder (5,4.6%) and malignancy (1,0.9%).

Most of the patients didn't had a significant personal history of substance abuse 62(57.4%) or any significant drug history 89 (82.4%).

Substance abuse

Statistically 46 (42.6%) had history of substance abuse of which alcoholism 46 (42.6%) prevailed more than smoking (19,17.6%).

Drug history

Data wise 17 (15.7%) patients had history of intake of oral contraceptive pills, 1 (0.9%) had steroid intake and 1(0.9%) had chemotherapy intake.

Investigations

Hemoglobin - Most of the patients had a hemoglobin level in the range of 7-10 gm% (64,59.3%), while 10 (9.3%) had a hemoglobin of less than 7gm% and 34 (31.5%) had a hemoglobin of more than 10gm%.

Total count - 55 (50.9%) had a total count of more than 11000 cells /mm³. ESR was high in 78 (72.2%).

PT-INR was elevated in 5 (4.6%), 25 (23.1%) had a high blood sugar level. Blood urea was increased in 7 (9.3%) and S. creatinine in 10 (9.3%), 21 (19.4%) had a deranged lipid profile, and 60 (55.6%) had dyselethrolytaemia, 4 (3.7%) were HIV positive. TSH levels were high in 12 (11.1%), and low in 2 (1.9%). A procoagulant state was present in 39 (35.8%) and connective tissue disorders in 16 (14.7%) cases. Presence of autoantibodies to detect connective tissue disorders - ANA was positive in 5 (4.6%), APLA in 14 (13%) while none showed Ds DNA positivity. Procoagulant state - S. Homocysteine was elevated in 26 (24.1%), and S. Fibrinogen in 1 (0.9%). No one showed presence of Factor v Leiden mutation while Protein C and S deficiency was present in 13 (12%) and Antithrombin 3 deficiency was present in 7 (6.5%).

Radiological features

X-ray paranasal sinus didn't show features of sinusitis in any of the cases. Infarct - was seen in 61 (56.5%) cases of which 39 (36.1%) had ischemic infarct and 22 (20.4%) had haemorrhagic infarct (Figure 2 - A and B).

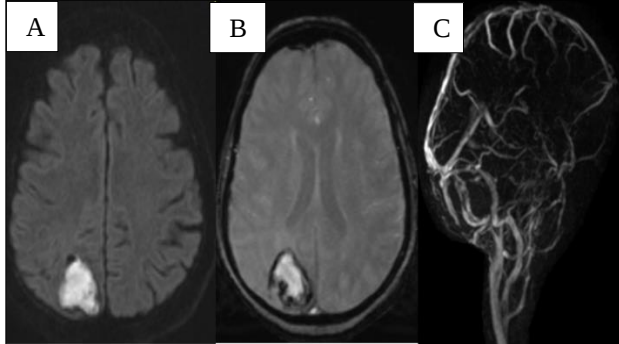


Figure 2: (A) Diffusion weighted (B) Susceptibility weighted Haemorrhagic venous infarct in the right parietal cortex (C) MR Venogram thrombosis of the Anterior 2/3rd superiorsagittal sinus.

Site of venous thrombosis

Superior sagittal sinus (81,75%) was the most common site for venous thrombosis (Figure 2C) followed by transverse sinus. Site of venous thrombosis and their frequency and percentage was listed in Table 2.

Modified Rankin Score (MRS) at admission, discharge and at follow up after 15 days

- MRS at admission / Baseline MRS of the patients ranged from 1- 4 of which a baseline MRS of ≤ 2 was

shown by 70 (64.8%) cases. A baseline MRS of 1 was shown by 50 (46.3%), 2 by 20 (18.5%), 3 by 33 (30.6%) and 4 by 5 (4.6%).

- MRS at discharge ranged between 0 and 6. An MRS of 0 was shown by 56 (51.9%), 1 by 29 (26.9), 2 by 19 (17.6%) and 6 by 4 (3.7%).
- MRS at follow up after 15 days ranged from 0 to 6 of which an MRS of 0 was shown by 79 (73.1%) 1 by 21 (19.4%), 2 by 4 (3.7%) and 6 by 4 (3.7%).

Table 2: Site of venous thrombosis with its frequency and percentage.

Site of venous thrombosis		Frequency	Percentage
Sigmoid sinus	Right	32	29.6
	Left	35	32.4
Superior sagittal sinus		81	75
Transverse sinus	Right	44	40.7
	Left	46	42.6
Straight sinus		10	9.3
Deep venous system		16	14.8
Cortical veins		18	16.7
Jugular veins		25	23.1

Outcome

- Primary outcome was taken as outcome during discharge. Good outcome (MRS of 0) was shown by 56(51.9%) bad outcome (MRS of 1-6) was shown by 52 (48.1%).
- Secondary outcome was taken as outcome during follow up after 15 days. Good outcome (MRS of 0) was shown by 77 (71.3%) and bad outcome (MRS of 1-6) was shown by 31 (28.7%).

Table 3: Univariate and multivariate analysis table of outcome at discharge.

Variable	Label	Outcome		Univariate regression		Multivariate regression	
		Good	Bad	p value	Odds ratio	p value	Odds ratio
Papilledema	Present	9	17	0.047	2.537	0.491	0.220
	Absent	47	35				
Head ache	Present	55	1	0.023	0.087	0.348	0.071
	Absent	43	9				
Glasgow coma Scale	15	52	4	0.002	6.314	0.841	1.526
	<15	35	17				
Focal neurological deficits	Present	50	6	0.000	0.049	0.922	0.661
	Absent	15.0	37				
Hypertension	Present	17.0	39	0.021.	3.324	0.019	65.439
	Absent	6	4				
Baseline MRS	≤ 2	48	8	0.000	0.028	0.000	0.004
	>2	2.0	50				
Infarct	Present	56	0	0.000	0.040	0.628	2.713
	Absent	52	0				

Table 4: Univariate and multivariate analysis table of outcome at 15 days after discharge.

Variable	Label	Outcome		Univariate regression		Multivariate regression	
		Good	Bad	p value	Odds ratio	p value	Odds ratio
Papilledema	Present	77	0	0.027	2.824	0.625	1.459
	absent	33	0				
Glasgow coma Scale	15	67	10	0.010	3.685	0.720	0.765
	<15	20	11				
Focal Neurological deficits	Present	59	18	0.000	0.073	0.281	6.153
	absent	06	25				
Baseline MRS	≤2	67	10	0.000	62.533	0.000	0.022
	>2	3	28				
Infarct	absent	77	0	0.000	0.068	0.919	0.921
	Present	33	0				

Factors which significantly affect the outcome at discharge and follow up after 15 days

- Univariate logistic regression was done to study the factors which significantly affect the outcome.
- At discharge - Head ache, Papilledema, Focal neurological deficits, Glasgow coma scale, hypertension, Baseline MRS and infarct has shown a significant association with outcome at discharge out of which only Hypertension and Baseline MRS emerged as a significant factor in predicting the outcome (Table 3).
- At follow up after 15 days -Papilledema, Focal neurological deficit, Glasgow coma scale, infarct, Baseline MRS and infarct showed significant association with the outcome in univariate analysis but on multivariate analysis only Baseline MRS had become an independent risk factor in predicting the outcome (Table 4).

DISCUSSION

CVT was earlier considered as a disease of females, as demonstrated by many previous studies done abroad and in India and especially occurred during pregnancy and puerperium but studies done nowadays showed male preponderance with alcoholism and hyperhomocysteinemia as predominant risk factors and is usually seen in young individuals.¹¹⁻²⁰ Study also proved same findings with preponderance of disease in young males. In contrast to some other studies done in India which showed a predominant sub acute mode of onset, our study most of the patients had acute onset of disease.^{1,21}

In this study headache followed by focal neurological deficits were the most common symptoms. Most of the previous studies conducted had similar finding with head ache only or with other neurological deficits as the most common clinical presentation.^{1,20} Many others studies hyperhomocysteinemia, alcoholism, procoagulant state, infections, OCP use, anaemia, level of consciousness,

thrombosis of deep venous system etc. emerged as common risk factors. But presence of hypertension was proved as an independent risk factor in our study in addition to the Baseline MRS which was also showed as risk factor by many other studies.¹⁻²² One previous study done in India had shown hypertension as a risk factor for CVT during pregnancy.²³ This study proved hypertension as a risk factor in general population also. Cerebral infarction was noticed in almost 56% of our cases which was comparable with many other studies.^{1,21} But in these studies, haemorrhagic infarct was predominant while in this study ischemic infarct was common. Like as noticed in many other studies, our study also the most common site of venous thrombosis was superior sagittal sinus.^{1,22,23}

Most of the patients (71.3%) had recovered completely and had a good outcome on short term follow up in our study which was comparable to many other studies.^{9,18,22,23} At the end of the follow up period death rate was only 3.7% which was impressive compared to some other studies 18 done in India.

CONCLUSION

From the above study we conclude that there had been an increase in the patients with acute onset of symptoms now. Hypertension has emerged as an independent risk factor for CVT in this study which was to be given due importance because many of the recent studies showed an increased prevalence of hypertension in Indian population which can also probably account for increased incidence of CVT. Our study also emphasized that the prognosis of CVT was becoming more and more favorable.

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

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APPENDIX - 1

Modified Rankin Scale (MRS)

Patient Name: _____

Rater Name: _____

Date: _____

Score -

Description

- No symptoms at all
- No significant disability despite symptoms; able to carry out all usual duties and activities
- Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
- Moderate disability; requiring some help, but able to walk without assistance
- Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
- Severe disability; bedridden, incontinent and requiring constant nursing care and attention
- Dead

Total (0–6): _____