

ORIGINAL RESEARCH

LONG-TERM OUTCOMES OF PATIENTS WITH CEREBRAL VENOUS SINUS THROMBOSIS FROM TAMIL NADU

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ABSTRACT

Background: Cerebral venous sinus thrombosis (CVST) is an important cause of stroke in young. There is paucity of literature on the long-term sequelae of CVST.

Methods: This hospital-based ambispective study included adult patients with radiologically confirmed CVST diagnosed between 2014 and 2020 with at least one year of follow up. We documented neurological disability at discharge and at follow-up using modified Rankin score (mRS), daily activity using Barthel index, cognitive deficits using Montreal Cognitive Assessment score (MOCA), the behavioral outcome with Hamilton depression rating scale (HDRS). Univariate and multivariate analyses were performed for factors presumed to be associated with outcomes.

Results: We identified 225 patients with CVST with a median age was 30 years (range 18-72), 117(52%) were women. Follow-up after a median of 24 months (range 12-63), 208(94.1%) scored 0-2 on mRS; however, cognitive impairment was seen in 104(69.1%), depression in 125(58.4%). On univariate analysis, factors associated with a poor motor outcome (mRS score 3-5) were low socioeconomic status, older age, diabetes mellitus, hypertension, migraine, frontal lobe involvement, baseline mass effect, and mRS at admission. On multivariate analysis, acute phase mass effect ($p=0.006$) (OR 49.4. CI 3.02-806.6), baseline mRS ($p=0.004$) (OR 53.3 CI 3.5-794.7) had a significant association. Low socio-economic status alone was associated with cognitive impairment ($p=0.002$). Univariate factors related to depression were puerperal CVST patients, anemia, disability, and mass effect at presentation, but only anemia ($p=0.066$) and the mass effect ($P=0.077$) had a multivariate association.

Conclusion: In one of the largest series long term follow up of CVST, though mortality and motor outcome were excellent, long-term neuropsychiatric impairment was common. Acute care and long-term management must have plans to prevent and manage these occult neuropsychiatric deficits.

Keywords: Cerebral venous sinus thrombosis, stroke, long term sequele

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is rare compared with arterial stroke, and it often occurs in young people. CVST accounts for up to 1% of all strokes worldwide.⁽¹⁾ However, Indian studies have documented a higher incidence of CVST. In hospital-based studies from India, 15-20% of stroke patients less than 40 years had CVST.⁽²⁾ Though most patients have an excellent outcome if treated early and appropriately, diagnosis may get delayed by the broad clinical spectrum of symptoms, various forms of initial presentation, obscuring of symptoms and signs by the underlying disease like meningitis, and often near-normal findings in neuroimaging.⁽³⁾ Significant interest exists around multiple treatment decisions—choice of anticoagulant, duration of therapy, the role of neuroimaging in therapeutic decision-making.⁽⁴⁾ Residual impairment of physical, psychological, social, and cognitive functions can occur secondary to sequelae of CVST due to infarctions, seizures, and raised intracranial tension.⁽⁵⁾ However, in identifying the best evidence-based treatment strategies for CVST, we will also need to determine the best primary outcomes to evaluate these therapies.

We conducted an ambispective study in a series of 225 patients with CVST to identify the clinical presentations, radiological features, and prognostic factors that predict a poor outcome in patients with CVST.

MATERIALS & METHOD

This study is a ambispective analysis of 225 patients admitted to our institution during the last 5 years. Patients diagnosed as CVST in the department of Neurology, Medicine and Obstetrics & Gynecology with confirmed clinical and radiological criteria were included in this study.⁽¹⁾ Ethics approval for the research was taken from Institute Ethics Committee (JIP/IEC/2018/400;31.12.2018). The study's main objective was to evaluate long-term motor, cognitive, and behavioral outcomes of cerebral venous sinus thrombosis and correlate with predictive factors.

Electronic data of patients with CVST from Oct 2014 to Oct 2019 were accessed to identify subjects who met our criteria. Prospectively we collected data from those who were admitted in JIPMER from 2019. Informed consent was taken. Demographic and epidemiological profile, clinical features, and follow-up data of patients were acquired from the electronic data base of the hospital information system of JIPMER. If the patients was not willing to follow up, telephonic interviews were used to assess the outcome by verbal questionnaires from the patients or immediate caretakers. Socioeconomic status was calculated using Modified Kuppuswamy scale.⁽⁶⁾ Neurological deficit or best guess neurological deficit at admission and discharge were recorded in descriptive terms at discharge and at follow up as MRS 0-6,⁽⁷⁾ daily activity at discharge and at follow up as Barthel index⁽⁸⁾ Cognitive deficits as Montreal Cognitive Assessment score (MOCA)⁽⁹⁾ or Telephonic MOCA(T-MOCA),⁽¹⁰⁾ Behavioural outcome as Hamilton depression rating scale (HDRS).⁽¹¹⁾ Functional outcome was categorised using the modified Rankin Scale⁽¹²⁾ as complete recovery (Rankin 0–1), partial recovery independent (Rankin 2), dependent (Rankin 3, 4 or 5) and death (Rankin 6). Brain imaging and neurovascular imaging data were extracted from archived images from 2014 and reported systematically by a neuroradiologist. Motor, cognitive and behavioural outcomes were correlated with risk factors, MR imaging pattern, and neurovascular pattern.

Statistical Analysis

Chi-square test was used to study the association between categorical variables. Correlation between predictive and outcome continuous variables were done using Pearson/Spearman correlation or using univariate regression and those between categorical predictors and outcome

variables by using logistic regressions. Dichotomised outcome variables like good (modified Rankin score [mRS] 0-2) versus poor outcome (3-6) ⁽¹³⁾ were analyzed using logistic regression. Confounding parameters were analyzed using multivariate analysis with a stepwise entry of confounding predictive variables found significant on correlation/univariate regressions. A p value of 0.05 or less was considered significant. All statistical analysis was carried out using SPSS v22.

RESULTS

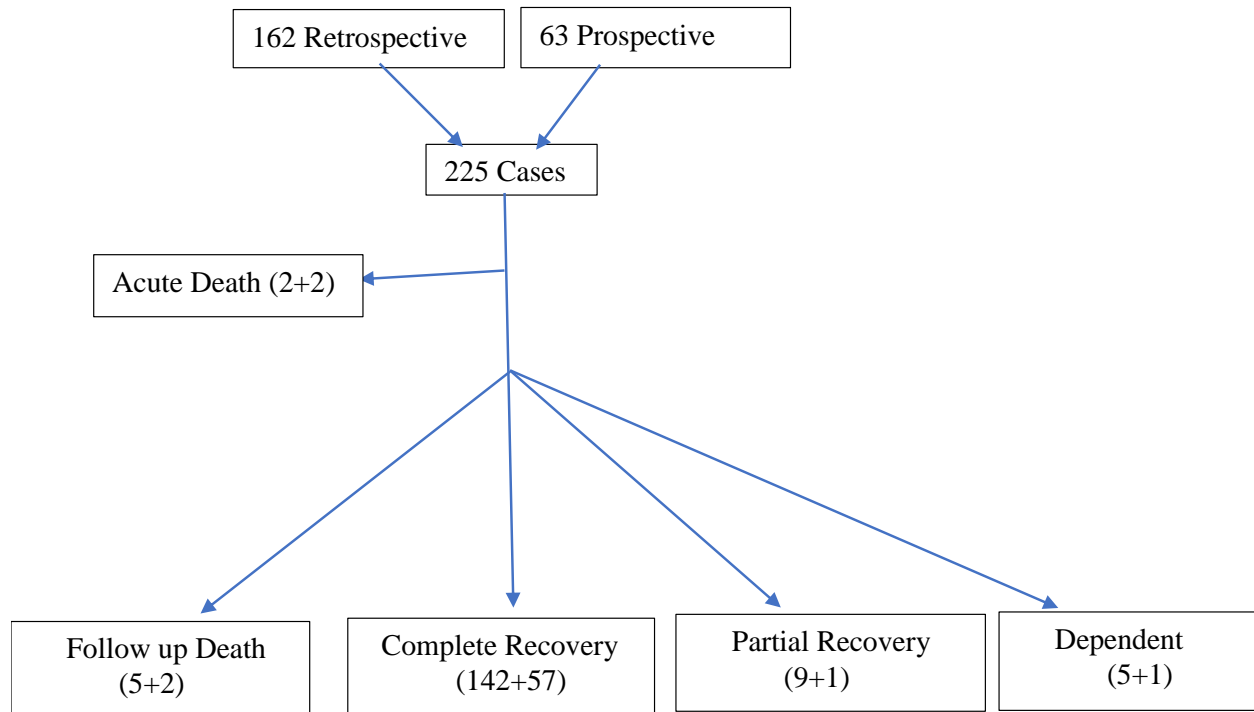


Fig- 1: Flow diagram of recruited patients

A total of 225 patients (retrospective-162, prospective-63) were included in this study with the diagnosis of CVST. Out of 225 patients with CVST, 108(48%) were men; mean age was 38.1(SD,11.3) years for men and 29.3(SD,11.4) years for women, respectively. 80% of the patients were Tamilian South Indians, 15% from neighbouring South Indian states and rest from the rest of India migrants settled in the Arcot region of the union territory of Pondicherry and Tamilnadu state and the rest mixed populations of migrants from other parts of India. The median follow-up period for the retrospective group was 31.5 months, and the prospective group 12 months. In our series, 186 (82.6%) patients were aged less than 45 years. 41% belonged to lower-middle socioeconomic status, upper-middle and upper socioeconomic group constituted 41%. Anemia was found in 56% of patients with mean hemoglobin of 11.6±3.6, 18.7% were obese with a median BMI of 23.6(15-44). Anemia was found more common in females (p<0.0001) and in the younger age group(p=0.005). Age and gender-wise, there was no significant difference in obesity. 8.8% of patients were diabetic, and 9.7% had hypertension. Diabetes mellitus was more common in males (p=0.01) and older age CVT patients(p<0.0001). There was no difference in hypertension among males and females, but hypertension was more common among older CVST patients(p<0.0001). 46 (39%) out of 117 patients had a diagnosis of CVST during the peripartum period, 6(5%) patients

developed CVST during pregnancy; all were during the third trimester.24(20.5%) were using contraceptive pills or hormonal therapy at the time of presentation. Active infection (tuberculosis(9),dental abscess(5), CSOM (16)) were found in 13.3% of patients. 2 patients had history of malignancy(breast cancer, Acute lymphocytic leukaemia).One patient underwent incision and drainage for parotid abscess within two months of presentation of CVST.

Table-1 : Baseline characteristics

	Male(108)	Female(117)	Total (225)	P value	OR,95%CI
Gender	N (%)	N(%)	N(%)		
Age (Mean and SD)	38.1(11.3)	29.3(11.4)	33.5(11.4)		
Young-onset (<45 yrs.)	78(72.2)	108(92.3)	186(82.6)	<0.001	3.6,1.79-7.25
Causes					
DM	15(13.8)	5(4.6)	20(8.8)	0.01	3.2,1.22-8.64
HTN	14(12.9)	8(6.8)	22(9.7)	0.12	1.8,0.82-4.34
Smoking	66(29.3)	0(0)	66(29.3)	<0.001	35.7,8.97-142.42
Alcohol	67(29.7)	0(0)	67(29.7)	<0.001	24.1,7.84-74.65
Migraine	16(14.8)	21(17.9)	37(16.4)	0.52	1.03,0.92-1.16
Malignancy	1(0.9)	1(0.8)	2(0.8)	1.0	0.99,0.92-1.02
Surg Within 3 Months	1(0.9)	0(0)	1(0.4)	0.48	0.99,0.97-1.01
Active Infection	13(12)	13(11.1)	26(11.5)	0.82	0.99,0.9-1.08
Anemia	33(30.5)	93(79.5)	126(56)	<0.001	3.3,2.32-4.94
Overweight	41(37.9)	52(44.4)	93(41.3)	0.77	0.90,0.46-1.77
Obese	21(19.4)	21(17.9)	42(18.6)	0.32	1.3,0.76-2.22
Pregnancy	0(0)	6(5.1)	6(5.1)		
Postpartum	0(0)	46(39.3)	46(39.3)		
Clinical Features					
Headache	52(48.1)	75(64.1)	127(56.4)	0.01	1.4,1.06-1.96
Vomiting	20(18.5)	29(24.7)	49(21.7)	0.25	1.1,0.94-1.21
Coma	3(2.7)	4(3.4)	7(3.1)	1.0	1.0,0.96-1.05
Seizure At Onset	58(53.7)	54(46.1)	112(49.7)	0.25	0.86,0.66-1.12
Late-Onset Seizure	2(1.8)	0(0)	2(0.8)	0.23	0.98,0.95-1.1
Aphasia	2(1.8)	0(0)	2(0.8)	0.23	0.98,0.95-1.01
Hemiplegia	15(13.8)	14(11.9)	29(12.8)	0.67	0.97,0.88-1.08
Cortical Blindness	1(0.9)	1(0.8)	2(0.8)	1.0	0.9,0.97-1.02
Morphology					
Normal	38(35.1)	45(38.4)	83(36.8)	0.61	1.15,0.67-1.98
Infarct	21(19.4)	37(31.6)	58(25.7)	0.03	1.9,1.03-3.55
Hemorrhage	12(11.1)	9(7.6)	21(9.3)	0.37	0.67,0.27-1.65
Haemorrhagic Infarct	37(34.2)	26(22.2)	63(28)	0.06	0.57,0.32-1.03
Sinus Involved					
SSS	86(79.6)	67(57.2)	153(68)	<0.001	1.4,1.15-1.67
TS	67(62)	74(63.2)	141(62.6)	0.85	1.1,0.73-1.45
SS	34(31.4)	41(35.04)	75(33.3)	0.57	1.1,0.87-1.27
ST	8(7.4)	69(5.1)	14(6.2)	0.48	0.9,0.91-1.05

Headache and seizure at onset were the most common presenting features. 127 (56%) patients presented with symptoms of headache, 112 (49%) with seizure at onset, 49 (21%) had vomiting, 29 (12.8 %) with hemiplegia. The most common sinus involved is superior sagittal sinus

150(66%), followed by transverse sinus 134(60%). More than one sinus was involved in 130 (57.8%) patients. The frontal lobe (20.4%) was the most common brain area affected. 28% had hemorrhagic infarct, and 44 (19.1%) had a mass effect.

Table-2: Death and Dependency during follow up of patients with cerebral venous thrombosis

	Male (N=108)(%)	Female (N=117)(%)	Total (N=225)
mRS at presentation*			
0-2	87(80.5)	101(86.3)	188(83.5)
3,4,5	20(18.5)	13(11.1)	33(14.6)
mRS at follow up#	N=107	N=114	N=221
0-2	99(92.5)	109(95.6)	208(94.1)
3,4,5	5(4.6)	1(0.8)	6(2.7)
Barthel Index at follow up	N=104	N=110	214
Normal (100)	93(89.4)	100(90.9)	193(90.2)
Slight dependency(91-99)	0(0)	1(0.9)	1(0.5)
Moderate dependency(61-90)	7(6.7)	8(7.3)	15(7)
Severe dependency(21-60)	4(3.8)	0(0)	4(1.9)
Total dependency(0-20)	0(0)	1(0.9)	1(0.5)
Death			
Death in Acute phase	1(0.9)	3(2.5)	4(1.8)
Death at follow up	3(2.8)	4(3.5)	7(3.2)
Timing of Death(Mean age in years and time in months from CVST)	47.6,17.1	36.5,21	

*225 patients

#221 patients

Functional outcome was good in 92.4% of patients scoring 0–2 on the mRS at follow-up, and there was gender-wise no significant difference in functional outcome. Hypertension, diabetes mellitus, frontal lobe involvement, hemorrhagic infarct, mass effect, headache at presentation were associated with poor functional outcome at discharge and follow up. The previous history of migraine(p=0.012) and sigmoid sinus(p=0.05) involvement had poor mRS scores on follow-up. Multivariate regression analysis showed factors predicting with poor functional outcome at discharge were hypertension (OR 7.7, CI 1.1-54.5, P = 0.03), presence of mass effect (OR 5.6, CI 1.1-27.3, P = 0.03) and at follow up only mass effect at presentation(OR 49.4, CI 3.026-806.6, P = 0.006). Twenty-one patients (9.3 %) required assistance in daily living activities (scoring below 100 points on the Barthel index). Univariate factors associated with dependency were presence of haemorrhagic infarct at presentation(p=0.003),frontal lobe involvement(p=0.012),with mass effect(p<0.0001),aphasia(p=0.008) and poor mRS at presentation(p<0.0001). On multivariate regression analysis, none of them were significantly associated.

Eleven (4.9%) patients died, out of which four patients succumbed in the acute phase. Gender wise there was no significant difference in mortality rate. Other factors predicting mortality were diabetes mellitus(p=0.001),hypertension(p=0.0020) at presentation, frontal lobe involvement(p=0.006) and vomiting as presenting feature(p=0.015). The majority of patients who

succumbed had SSS, transverse, and multiple sinus involvement. A total of 8 (3.5%) patients were required neurosurgical intervention in the form of decompressive craniectomy.

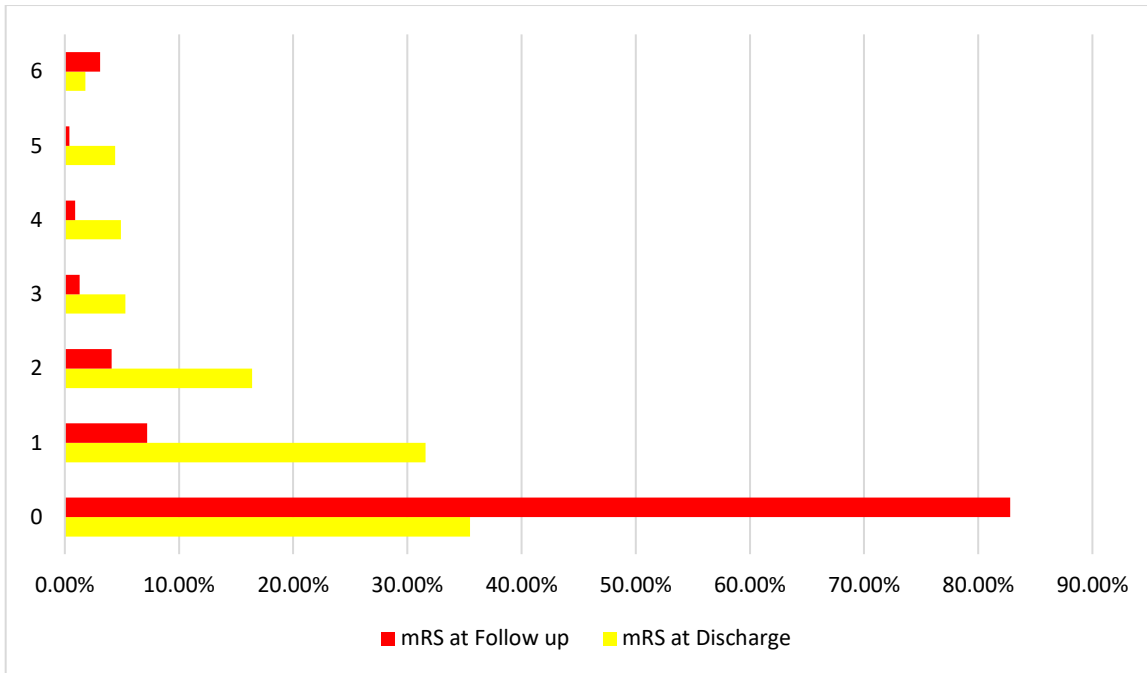


Figure -3: Motor outcome at Follow up

Table-3: Events during follow-up

Thrombotic events	
Recurrent cerebral venous thrombosis	4(1.7)
Deep vein thrombosis	2(0.9)
Pulmonary embolism	1(0.4)
Residual symptoms	
Headache	43(19.1)
Aphasia	1(0.4)
Motor deficit	6(2.6)
Impaired vision	1(0.4)
Epilepsy	23(10.2)

Two hundred fourteen patients were assessed with the neuropsychological battery(MOCA(114) or T-MOCA(100)) at a median 24(range 12-63) months after CVST. Cognitive impairment was observed in 148(69.1%) patients. Among 208 patients with good mRS, 142 (68.2%) had cognitive impairment, and among six patients with poor mRS, all were cognitively impaired. 73(70%) male patients, and 75(68%) female patients had cognitive impairment. Out of 20 patients who require assistance in daily activity(BI<100), 19 were cognitively impaired(p=0.009) and among depressed patients, 94(75.2%) had cognitive impairment(p=0.023). There was an increased presence of cognitive impairment in the low socioeconomic status group(p=0.008).

Scores on the HDRS scale were normal in 89(41.6) patients.109(50.9%) patients had mild depression,13 (6.1%) had moderate depression, and 3 (1.4%) had severe depression without any significant gender difference(p=0.23). Among 43 patients with persistent headaches, 24 had

depression. Twenty-three patients had a recurrence of seizures, of whom thirteen were depressed. Out of the 125 patients with depression, 49(39.2%) were anemic at presentation. Eighteen of the forty-eight patients (37.5%) with postpartum CVST had depression. There was increased presence of depression in patients with anaemia at presentation($p=0.006$), postpartum CVST($p=0.014$), seizure at onset($p=0.037$), parietal lobe involvement($p=0.01$), with mass effect on brain imaging($p=0.019$), higher mRS at discharge ($p=0.04$). Among 185 patients with good mRS, 103 (55.6%) were depressed, and among 29 patients with poor mRS, 22 (75.8%) were depressed. The factors predictive for depression on multivariate analysis ($p<0.1$) were anaemia at presentation (OR 0.5, CI 0.29-1.04, $P = 0.06$) and postpartum CVST(OR 0.5, CI 0.23-1.07, $P = 0.07$).

Table-4: Depression and cognitive impairment in patients with cerebral venous thrombosis

	Male (N=104)(%)	Female (N=110)(%)	Total (N=214)(%)61.5)
HDRS			
HDRS (Tel.) Median , Range	8,2-24	8,2-20	8,2-24
HDRS (Nor.) Median , Range	10,1-23	8,1-30	9,1-30
Normal	40(38.4)	49(44.5)	89(41.6)
Depression	64(61.5)	61(55.4)	125(58.4)
Mild	57(54.8)	52(47.2)	109(50.9)
Moderate	5(4.8)	8(7.2)	13(6.1)
Severe	2(1.9)	1(0.9)	3(1.4)
MOCA			
T-MOCA, Median, Range	14,4-21	15,8-21	17,4-21
MOCA, Median, Range	18,5-28	19,3-29	26,3-29
Cognitive impairment	73(70.2)	75(68.2)	148(69.1)

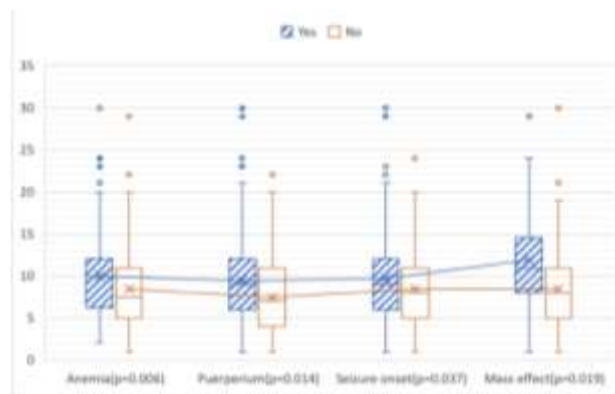


Fig- 2: HDRS score distribution

DISCUSSION

In this large cohort study despite of good functional recovery, we found that most them had cognitive impairment at follow up. Anemia at presentation and post-partum CVST were the strong predictor of depression at follow up. In this study, a total of 225 patients with Radiological features of cerebral venous thrombosis were evaluated over five years. 108 out of 225 patients were male, and the remaining were female. This study of 225 patients with CVST cannot give precise information about the disease's real incidence. Also, it cannot make any generalization of the results to the whole Country as it includes only Tamilian patients. Comparison of clinical and

etiological features of various Indian and Western countries large series with our study is given in the following table.

Table- 5: Comparison of baseline variable with different studies.

	Parikh et al (14)	Narayan et al (15)	Ferro et al ⁽¹⁶⁾	Wassay et al ⁽¹⁷⁾	Present study
Year published	1987	2012	2004	2008	-
Country	India	India	21 Countries	United States	India
Number of patients	110	428	624	182	225
Study design	Case series	Prospective case series	Prospective multicenter cohort	Multicenter ambispective cohort	Single-center ambispective cohort
Mean Age	na	31.3 years	39.1 years	38 years	33.5 years
Male: Female	2:1	1.16:1	1:2.92	1:1.5	1:1.08
Clinical presentation					
Headache	38.1%	88.3%	88.8%	71%	56.4%
Vomiting	na	na	Na	na	21.7%
Papilledema	29%	63.4%	28.3%	32%	na
Aphasia	na	na	19.1%	5%	0.8%
Seizure	60%	39.9%	39.3%	32%	49.7%
Paresis	38.1%	27.7%	37.2%	41%	12.8%
Coma	17.2%	10.4%	13.9%	20%	3.1%
Blindness	na	na	Na	na	0.8%
Fever	30.3%	5.4%	Na	14%	na
Etiological factor					
Anemia	na	na	na	na	57.7%
Obesity	na	na	na	na	18.6%
Oral contraceptives	0.9%	11.4%	54.3%	5%	20.5%
Pregnancy or puerperium	2.7%	9.8%	20.1%	7%	44.4%
Acquired prothrombotic condition	na	na	15.7%	4%	na
Infection	na	2.1%	12.3%	1.6%	13.3%
Malignancy	na	0.9%	7.4%	7%	0.8%

na – not applicable

In the present cohort, in addition to conventional risk factors postpartum (39%), smoking (30%), alcoholic (31%), OCP pill use (20%), HTN(10%), DM (9%) are significant risk factors, 56 % of patients were anemic at presentation, whether this is a reflection of a high incidence of anemia in Indian population particularly in pregnant females or anemia is a real risk factor needs further evaluation. The present series also reflects our interest in infection as in our study, active infections were found in 13.3% of patients. Nagarajan *et al* found that infection was present in 28% of cases.⁽¹⁸⁾

The standard treatment for CVST is heparin, and most patients recover well with this therapy. Lath *et al.* stated that the mortality in CVST, in addition to progressive thrombosis, is related to elevated intracranial pressure causing transtentorial herniation. ⁽¹⁹⁾They reported a mortality of 27%. These findings are comparable with our result with low mortality of 4.9%. Small retrospective case series suggest that decompressive hemicraniectomy can be lifesaving in patients with cerebral venous thrombosis and impending brain herniation.⁽²⁰⁾⁽²¹⁾ A retrospective multinational registry of acute CVST cases undergoing decompressive surgery included 38 patients. Twelve patients (32%) recovered completely [modified Rankin Scale (mRS) 0–1], and only three patients (8%) were severely dependent (mRS 4–5). Six patients (18%) died.⁽²²⁾ In our study, 44 (19.1%) patients had a mass effect, out of which eight patients had undergone decompression hemicraniectomy. Two patients (25%) recovered completely [modified Rankin Scale (mRS) 0–1], two patients (25%) were severely dependent (mRS 4–5), and two patients (25%) died.

The recurrence of venous thromboembolism (3.1%) in our study was lower than that observed in previous studies in which 6 % of patients suffered from VTE and CVST recurred in 1.7% of patients. In contrast, CVST recurrence in the ISCVT study was 2.2%. We found a 10 % rate of active epilepsy at follow up, similar to that in previous studies.⁽²³⁾⁽²⁴⁾⁽²⁵⁾ As many as 19% of our patients reported suffering from headache more than once a week; in previous studies, the prevalence of residual headache has varied widely from 10 to 50 percent .⁽²⁶⁾⁽¹²⁾⁽²⁷⁾

Our findings on mortality and functional outcome are similar to the results of the largest study on CVST study to date, the ISCVT with <10 % mortality and 80 % of patients achieving good functional recovery (mRS 0-1). (26)Dependency (Barthel Index<100) was low, with only 9.9 % of patients requiring help in daily activities. Multivariate methods in previous studies analyzed long-term prognostic factors ⁽²⁵⁾⁽⁵⁾confirmed coma, cerebral hemorrhage, and malignancyas significant prognostic factors for dependence. We identified mass effect, hemiplegia, mRS at presentation were increase the risk of dependency. Comparison between different studies is shown in the table.

Table-6: Comparison death and dependency with other studies

	No. of patients	Acute Phase Mortality no. (%)	Outcome at 1 year or more, no. of patients		
			Total	Death	Level of disability
Ferro et al, Multicentric,2002 ⁽¹²⁾	142	9 (6.3)	126	2	mRS 0-1: 108,mRS 2:12 mRS 3-5: 4
Stolz et al, Germany,2005 ⁽²⁸⁾	79	12(15.2)	58	2	mRS 0-1: 50,mRS 2-3:2 mRS 4-5: 4
Breteau et al, France,2003 ⁽²⁵⁾	55	4(7.3)	51	3	mRS 0-2: 45, mRS 3-5: 3
Ferro et al, Multicentric ,2005 ⁽²⁹⁾	626	27(4.3)	582	10	mRS 0-1: 493,mRS 2:47 mRS 3-5: 32
Present study, India	225	4	221	7	mRS 0-2:208, mRS 3-5: 6

Depression has been documented in two-thirds of patients with CVST.⁽³⁰⁾ We found that depression was prevalent in 58.4% of CVST patients on follow up.37.5% of postpartum CVST had depression on follow up, and it was also significantly associated with depression(p=0.014). A systematic review of studies in 11 high-income countries showed that, based on point prevalence estimates, around 12.9% (95% CI: 10.6– 15.8) of mothers were depressed at three months postpartum.⁽³¹⁾ A meta-analysis done by Ravi Prakash Upadhyay et al. depression among

postpartum women found that the prevalence of depression among Indians mothers was 22% (95% CI: 19–25).⁽³²⁾ The estimated overall pooled prevalence was highest in the southern region of the Country (26%) followed by eastern (23%), western (21%), then least in northern (15%). A cross-sectional study by Vanishree Shiram et al in a rural population of Tamil Nadu, India, found that the prevalence of depression during the postpartum period was 11%.⁽³³⁾ These data confirm that prevalence of depression postpartum CVST is more as compared to without. This should be identified early and treated promptly. Depression has been demonstrated in 18% using Beck's depression inventory among 34 patients included in another study, and none of them had a cognitive or functional disability.⁽³⁴⁾ But we found that out of 148 cognitively impaired, 94 (63.5%) had depression. So it is essential to evaluate the cause of depression in patients with CVST despite having good mRS.

Jean-Marc Bugnicourt et al one observational study in two centers in France showed that cognitive impairment was observed in 31 % of the CVST survivors.⁽³⁵⁾ There was limited data on cognitive impairment after CVST. Various studies have reported varied cognitive impairment, 3.5% in Himachal Pradesh,⁽³⁶⁾ 5.1% in Uttar Pradesh,⁽³⁷⁾ 6.5% in Kashmir,⁽³⁸⁾ and 11.5% in Kerala, South India.⁽³⁹⁾ As compared to these studies in our study, cognitive impairment was found in 69.1%, which is significantly higher than the general population. This can be attributed to CVST. There was no gender preponderance. Patients who were of low socioeconomic status, depressed at follow-up, and requiring assistance for daily activity were more cognitively impaired.

Our study is among the largest published single-center series on CVST outcome thus far, in a single ethnic group, namely Tamilians, with a long follow-up period. The long term data on cognitive and behavioural outcome also make it unique

CONCLUSION

Our study reinforces the finding that long-term motor outcome after CVST is good, with most patients achieving independence and a low risk for recurrent CVST at least in the first few years of follow up. However, long-term neuropsychological impairment was surprisingly common. Acute care and long-term management must strategise plans to prevent and manage these occult neuropsychological deficits.

REFERENCES

1. Bousser M-G, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol*. 2007 Feb;6(2):162–70.
2. Dash D, Prasad K, Joseph L. Cerebral venous thrombosis: An Indian perspective. *Neurol India*. 2015 May 1;63(3):318.
3. Ameri A, Bousser M-G. Cerebral Venous Thrombosis. *Neurol Clin*. 1992 Feb 1;10(1):87–111.
4. Coutinho JM, de Bruijn SFTM, de Veber G, Stam J. Anticoagulation for cerebral venous sinus thrombosis. *Stroke*. 2012 Apr;43(4):e41–2.
5. de Bruijn SF, de Haan RJ, Stam J. Clinical features and prognostic factors of cerebral venous sinus thrombosis in a prospective series of 59 patients. For The Cerebral Venous Sinus Thrombosis Study Group. *J Neurol Neurosurg Psychiatry*. 2001 Jan;70(1):105–8.
6. Wani RT. Socioeconomic status scales-modified Kuppaswamy and Udai Pareekh's scale updated for 2019. *J Fam Med Prim Care*. 2019 Jun;8(6):1846–9.

7. Bruno Askiel, Akinwuntan Abiodun E., Lin Chen, Close Brian, Davis Kristin, Baute Vanessa, et al. Simplified Modified Rankin Scale Questionnaire. *Stroke*. 2011 Aug 1;42(8):2276–9.
8. Della Pietra GL, Savio K, Oddone E, Reggiani M, Monaco F, Leone MA. Validity and reliability of the Barthel index administered by telephone. *Stroke*. 2011 Jul;42(7):2077–9.
9. Lees R, Selvarajah J, Fenton C, Pendlebury ST, Langhorne P, Stott DJ, et al. Test accuracy of cognitive screening tests for diagnosis of dementia and multidomain cognitive impairment in stroke. *Stroke*. 2014 Oct;45(10):3008–18.
10. Zietemann V, Kopczak A, Müller C, Wollenweber FA, Dichgans M. Validation of the Telephone Interview of Cognitive Status and Telephone Montreal Cognitive Assessment Against Detailed Cognitive Testing and Clinical Diagnosis of Mild Cognitive Impairment After Stroke. *Stroke*. 2017 Nov;48(11):2952–7.
11. Potts MK, Daniels M, Burnam MA, Wells KB. A structured interview version of the Hamilton Depression Rating Scale: evidence of reliability and versatility of administration. *J Psychiatr Res*. 1990;24(4):335–50.
12. Ferro JM, Lopes MG, Rosas MJ, Ferro MA, Fontes J, Cerebral Venous Thrombosis Portuguese Collaborative Study Group. Long-term prognosis of cerebral vein and dural sinus thrombosis. results of the VENOPORT study. *Cerebrovasc Dis Basel Switz*. 2002;13(4):272–8.
13. Chaisinanukul N, Adeoye O, Lewis RJ, Grotta JC, Broderick J, Jovin TG, et al. Adopting a Patient-Centered Approach to Primary Outcome Analysis of Acute Stroke Trials Using a Utility-Weighted Modified Rankin Scale. *Stroke*. 2015 Aug;46(8):2238–43.
14. Parikh PM, Sukthankar RU, Parikh A, Pipalia DH, Sidhva SJ, Ramakanten R, et al. Cerebral venous thrombosis. *J Assoc Physicians India*. 1987 May;35(5):349–51.
15. Narayan D, Kaul S, Ravishankar K, Suryaprabha T, Bandaru VCSS, Mridula KR, et al. Risk factors, clinical profile, and long-term outcome of 428 patients of cerebral sinus venous thrombosis: Insights from Nizam’s Institute Venous Stroke Registry, Hyderabad (India). *Neurol India*. 2012 Mar 1;60(2):154.
16. Ferro JM, Canhão P, Stam J, Boussier M-G, Barinagarrementeria F, ISCVT Investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke*. 2004 Mar;35(3):664–70.
17. Wasay M, Bakshi R, Bobustuc G, Kojan S, Sheikh Z, Dai A, et al. Cerebral venous thrombosis: analysis of a multicenter cohort from the United States. *J Stroke Cerebrovasc Dis Off J Natl Stroke Assoc*. 2008 Apr;17(2):49–54.
18. D N. Puerperal cerebral venous thrombosis : therapeutic benefit of low dose heparin. *Neurol India*. 1999 Jan 1;47(1):43.
19. Lath R, Kumar S, Reddy R, Boola GR, Ray A, Prabhakar S, et al. Decompressive surgery for severe cerebral venous sinus thrombosis. *Neurol India*. 2010 Jun;58(3):392–7.
20. Coutinho Jonathan M., Majoie Charles B.L.M., Coert Bert A., Stam Jan. Decompressive Hemicraniectomy in Cerebral Sinus Thrombosis. *Stroke*. 2009 Jun 1;40(6):2233–5.
21. Théaudin M, Crassard I, Bresson D, Saliou G, Favrole P, Vahedi K, et al. Should decompressive surgery be performed in malignant cerebral venous thrombosis: a series of 12 patients. *Stroke*. 2010 Apr;41(4):727–31.
22. Ferro JM, Crassard I, Coutinho JM, Canhão P, Barinagarrementeria F, Cucchiara B, et al. Decompressive surgery in cerebrovenous thrombosis: a multicenter registry and a systematic review of individual patient data. *Stroke*. 2011 Oct;42(10):2825–31.
23. Preter M, Tzourio C, Ameri A, Boussier MG. Long-term prognosis in cerebral venous thrombosis. Follow-up of 77 patients. *Stroke*. 1996 Feb;27(2):243–6.

24. Miranda B, Ferro JM, Canhão P, Stam J, Bousser M-G, Barinagarrementeria F, et al. Venous thromboembolic events after cerebral vein thrombosis. *Stroke*. 2010 Sep;41(9):1901–6.
25. Breteau G, Mounier-Vehier F, Godefroy O, Gauvrit J-Y, Mackowiak-Cordoliani M-A, Girot M, et al. Cerebral venous thrombosis 3-year clinical outcome in 55 consecutive patients. *J Neurol*. 2003 Jan;250(1):29–35.
26. Ferro JM, Canhão P, Aguiar de Sousa D. Cerebral venous thrombosis. *Presse Medicale Paris Fr* 1983. 2016 Dec;45(12 Pt 2):e429–50.
27. Strupp M, Covi M, Seelos K, Dichgans M, Brandt T. Cerebral venous thrombosis: correlation between recanalization and clinical outcome--a long-term follow-up of 40 patients. *J Neurol*. 2002 Aug;249(8):1123–4.
28. Stolz E, Rahimi A, Gerriets T, Kraus J, Kaps M. Cerebral venous thrombosis: an all or nothing disease? Prognostic factors and long-term outcome. *Clin Neurol Neurosurg*. 2005 Feb;107(2):99–107.
29. Canhão P, Ferro JM, Lindgren AG, Bousser M-G, Stam J, Barinagarrementeria F, et al. Causes and predictors of death in cerebral venous thrombosis. *Stroke*. 2005 Aug;36(8):1720–5.
30. Saroja AO, Thorat NN, Naik KR. Depression and Quality of Life after Cerebral Venous Sinus Thrombosis. *Ann Indian Acad Neurol*. 2020;23(4):487–90.
31. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. *Obstet Gynecol*. 2005 Nov;106(5 Pt 1):1071–83.
32. Upadhyay RP, Chowdhury R, Aslyeh Salehi, Sarkar K, Singh SK, Sinha B, et al. Postpartum depression in India: a systematic review and meta-analysis. *Bull World Health Organ*. 2017 Oct 1;95(10):706-717C.
33. Shriram V, Shah PB, Rani MA, Sathiyasekaran BWC. A community-based study of postpartum depression in rural Southern India. *Indian J Soc Psychiatry*. 2019 Jan 1;35(1):64.
34. Buccino G, Scoditti U, Patteri I, Bertolino C, Mancina D. Neurological and cognitive long-term outcome in patients with cerebral venous sinus thrombosis. *Acta Neurol Scand*. 2003 May;107(5):330–5.
35. Bugnicourt J-M, Guegan-Massardier E, Roussel M, Martinaud O, Canaple S, Triquenot-Bagan A, et al. Cognitive impairment after cerebral venous thrombosis: a two-center study. *J Neurol*. 2013 May;260(5):1324–31.
36. Sharma D, Mazta SR, Parashar A. Prevalence of cognitive impairment and related factors among elderly: A population-based study. *J Dr NTR Univ Health Sci*. 2013 Jul 1;2(3):171.
37. Poddar K, Kant S, Singh A, Singh TB. An epidemiological study of dementia among the habitants of eastern Uttar Pradesh, India. *Ann Indian Acad Neurol*. 2011;14(3):164–8.
38. Raina S, Razdan S, Pandita KK, Raina S. Prevalence of dementia among Kashmiri migrants. *Ann Indian Acad Neurol*. 2008 Apr;11(2):106–8.
39. Shaji S, Bose S, Verghese A. Prevalence of dementia in an urban population in Kerala, India. *Br J Psychiatry J Ment Sci*. 2005 Feb;186:136–40.