Original Article

Internal Medicine Section

A Study of the Clinical Features and the Outcome of Cerebral Venous Sinus Thrombosis in a Tertiary Care Centre in South India

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ABSTRACT

Background: Cerebral venous sinus thrombosis (CVST) is an uncommon cause of stroke, with extremely diverse clinical features, predisposing factors, brain imaging findings and outcomes. The prognosis of CVST is variable and its outcome may vary from recovery to permanent neurological deficits.

Aims: To study the clinical features, prognostic factors and the outcome in CVST.

Study Design: Prospective study.

Materials and Methods: Fifty patients with radiologically confirmed CVST were studied from November 2005 to October 2006. The demographical, clinical, radiological and outcome data were recorded and analyzed. The prognostic factors in patients who were enrolled in the study were prospectively investigated. A poor outcome after 12 weeks, which was defined as death or dependency (by the modified Rankin scale [mRS] ≥3), was used as the principal outcome measure.

Results: The most common presenting features were headache (90%), focal deficits (48%), seizures (44%), and coma (14%). Puerperium was the most common risk factor. After 12 weeks of follow up, nine patients (18%) had a poor outcome (mRS≥3or death). The multivariate predictors of a poor outcome were age >30 years, male sex, coma at presentation, cerebral haemorrhage and deep cerebral venous system thrombosis.

Conclusion: CVST can affect all age groups, particularly women of the child bearing age. The overall prognosis of CVST is fairly good with an independent survival of 82%.

Key Words: Clinical features, Outcome, Prognostic factors, Sinus thrombosis

KEY MESSAGE

- CVST can affect all age groups, particularly women of child bearing age.
- The post partum state and infections were the most common predisposing factors.
- The overall prognosis of CVST is fairly good, with an independent survival of 82%.

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a disease with potentially serious consequences, which usually affects young and middle aged people. CVST is rare as compared to arterial stroke. Its clinical evolution seems to be different from the other stroke subtypes and is highly variable between the studies [1].

Although it may present with a variety of signs and symptoms, headache is the most frequent and often the earliest manifestation [2]. Despite the improvements in its diagnosis and treatment, dural sinus thrombosis may still cause death or permanent disability. The outcome of the patients with cerebral venous sinus thrombosis may vary from complete recovery to permanent neurological deficits as a natural course of the disease [3].

In the acute phase, it is important to identify those patients who have a poor prognosis because this may influence the therapeutic strategy and enable the treating physician to give reliable information to the patient and his/her relatives.

In contemporary studies, the reported mortality rate was found to range between 8% and 14% [4]. This was in contrast to prior studies in which cause specific mortality was as high as 30% to 50% [5].

Reliable data on the natural history and the prognosis of CVST are scarce. This present study was planned to evaluate the clinical features, prognostic factors and the outcome in CVST.

MATERIALS AND METHODS

The present study included 50 cases of CVST which were admitted to the Department of Internal Medicine, Karnataka Institute of Medical Sciences, Hubli, South India, after considering the inclusion and exclusion criteria. The study spanned over a period of 12 months, from November 2005 to October 2006.

The reasons for exclusion were age younger than 12 years, indications or contraindications for heparin; and conditions with a poor prognosis which was unrelated to CVST.

All the patients underwent computerised tomography (CT) scan or magnetic resonance imaging (MRI) of the brain and were reviewed by trained radiologists. The diagnosis was based on established radiological criteria. Demographical, clinical, laboratory, and radiological data were recorded. The functional status was recorded on a modified Rankin scale(mRS) at admission, discharge and at 12 weeks follow-up and the outcome was dichotomized as good (score of 0–2) or poor (score ≥3).

The outcome was recorded at discharge from the hospital and at 12 weeks follow-up. In addition, the in-hospital mortality was recorded separately.

STATISTICAL ANALYSIS

χ^2 tests (or Fisher's exact test whenever appropriate) were performed to analyze the univariate relationship between the possible prognostic factors and the outcome at 12 weeks. As it was likely that the different prognostic factors were mutually related, the independent effects of the prognostic factors were additionally analyzed by using multivariate logistic regression. Subsequently, all the variables with p≤ 0.25 which were identified in the univariate analysis were presented to a logistic regression model to assess their independent prognostic values.

The significant prognostic factors were selected with a forward selection strategy by using the likelihood ratio statistic, with p ≤ 0.05 as the criterion level for selection. The effect sizes were expressed as the odds ratios (OR). The OR can be interpreted as an estimation of the relative risk of a poor outcome. The data was analyzed by the SPSS, version 14.0 (SPSS Inc).

RESULTS

Fifty cases (40 females and 10 males) were included in the study. The mean age of the study population was 29.06 years with a range from 14 to 54 years (median 30 years). Among the total study subjects, 42% of the patients were in the age group between 21-30 years.

The neurological symptoms and signs at admission are summarised in the [Table/Fig 1]. Headache was the most frequent symptom which was present in 45(90%) patients. Seven patients (14%) were presented in coma. Out of 50 cases, 28 cases (56%) had a sub acute onset. An acute and chronic onset was noted in 17(34%) and five (10%) cases respectively.

The risk factors for CVST are shown in [Table/Fig 2]. Twenty five (50%) patients were in puerperium and three patients (6%) had used oral contraceptive pills. No possible cause for CVST could be identified in 10(20%) patients.

All the patients underwent brain imaging. The most common modality which was used was MRI of the brain (73%), followed by CT scan of the brain (48%). Cerebral haemorrhage was found in 18(36%) patients and cerebral infarct was found in 36(64%) patients by CT or MRI. The superior sagittal sinus was the most

	n	%	Poor outcome (n=9)	Good outcome (n=41)	p value (χ^2 or Fisher's exact)	Odds ratio (Poor outcome)
Age						
≤ 30 years	31	62	2	29	–	–
> 30 years	19	38	7	12	<0.05	8.46
Sex						
Male	10	20	5	5	<0.01	9
Female	40	80	4	36	–	0.11
Symptoms and signs						
Headache	45	90	8	37	0.999	0.86
Focal deficits	24	48	6	18	0.281	2.56
Seizures	22	44	6	16	0.157	3.13
Papilloedma	20	40	5	15	0.454	2.17
Isolated intracranial hypertension	14	28	–	14	0.047	–
Impaired conciousness	12	24	3	9	0.668	1.78
Aphasia	10	20	2	8	0.999	1.18
Coma	7	14	6	1	<0.001	80
Visual impairment	5	10	1	4	0.999	1.16
CT/MRI lesions						
Cerebral infarct	32	64	2	30	>0.05	–
Cerebral haemorrhage	18	36	7	11	<0.03	24
Sinus involvement						
Superior sagittal sinus	41	82	7	34	0.657	0.72
Left lateral sinus	18	36	3	15	0.999	1.87
Right lateral sinus	16	32	3	13	0.999	1.07
Straight sinus	8	16	2	6	0.623	1.67
Deep venous system	5	10	4	1	0.002	32
Cavernous sinus	1	2	–	1	0.999	–

[Table/Fig-1]: Demographic, clinical, and imaging features of included patients

Risk factors	n	%	Poor outcome (n=9)	Good outcome (n=41)	p value (χ^2 or Fisher's exact)	Odds ratio (Poor outcome)
Puerperium	25	50	2	23	0.138	0.23
Idiopathic	10	20	4	6	0.065	4.67
Oral contraceptive pills	3	6	0	3	0.999	–
Ear, Nose & Throat infections	3	6	0	3	0.999	–
Polycythaemia	3	6	2	1	0.08	11.43
Dehydration	2	4	–	2	0.999	–
Homocystinaemia	2	4	1	1	0.331	5
Pregnancy	2	4	0	2	0.999	–

[Table/Fig-2]: Risk factors profile of included patients

Outcome	Number (n=50)	Percentage (%)
Outcome at discharge		
Good outcome (mRS<3)	40	80
Poor outcome (mRS≥ 3 or death)	10	20
Outcome at 12 weeks		
Good outcome (mRS<3)	41	82
Poor outcome (mRS≥ 3 or death)	9	18

[Table/Fig-3]: Outcome of the patients who were studied

Modified Rankin Scale	Out come at discharge		Outcome at 12 weeks	
	No. of cases	Percentage	No. of cases	Percentage
0	12	24%	20	40%
1	20	40%	15	30%
2	8	16%	6	12%
3	3	6%	3	6%
4	2	4%	1	2%
5	2	4%	1	2%
Death	3	6%	4	8%
Death or dependency	10	20%	9	18%

[Table/Fig-4]: Outcome of the patients at discharge and at 12 weeks follow-up

common sinus which was involved in 41(82%) patients, as shown in [Table/Fig 1].

In the acute phase, most patients (74 %) were anti coagulated with intravenous heparin or subcutaneous low molecular weight heparin (LMWH) in therapeutic dosages. Additional treatment included anti epileptic drugs, osmotherapy, steroids and acetazolamide and 6% of the patients required mechanical ventilation.

Information on the outcome at discharge and after 12 weeks of follow up was available for all the patients [Table/Fig 3].Ten patients were either dead (n=3) or disabled (mRS≥3; n=7) at the time of discharge. None of the patients with post partum CVST died.

The twelve week follow up was assessed by a face to face interview. None of the patients were lost to follow up. At the end of 12 weeks of follow up, four patients died (8%) and five (10%) patients remained dependent with mRS ≥3 [Table/Fig 4].

On a multivariate analysis, age >30 years ($p<0.05$), male sex ($p<0.01$), coma (GCS<9) at presentation ($p<0.001$), cerebral haemorrhage ($p<0.03$) on imaging and deep cerebral venous system involvement ($p<0.01$) were associated with a poor outcome at 12 weeks of follow-up. Isolated intracranial hypertension was associated with a good outcome ($p<0.05$).

DISCUSSION

The clinical presentation of CVST is extremely variable ranging from an isolated headache to focal deficits to encephalopathy to psychiatric manifestation to coma [6, 7]. Headache was the most common symptom which was seen in 90% of the patients and seven patients (14%) were presented in coma. de Bruijn SFTM et al reported that headache was seen in 95% of patients and coma in 15% of the patients [8].

In our study, 62.5% (25 out of 40) female patients were in the post partum period as opposed to <15% which was reported from the west [4,8,9]. A possible explanation for this difference may be home deliveries in unhygienic environments. In our study, only 6% of the women were using oral contraceptives. This was in contrast to studies from the west, where the use of oral contraceptives was implicated in 54 to 77% of the CVST cases [4, 8, 9].

Ear, nose and throat infections accounted for 6% of the CVST cases in our study, as compared to 8.2% in the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) [4]. Hyper homocystinaemia is an important cause of hypercoagulopathy which increases the risk of CVST by four fold [10]. In our study, plasma homocysteine was elevated in two patients and no cause for CVST was identified in 10(20%) patients.

We noted some significant differences in the risk factor profile for this disease from that of the west, i.e. in the post partum state, which was more common in our population. Oral contraceptive use was not a major risk factor in our setting. Only 74% of our patients received anticoagulation. This was lower than that which was reported by ISCVT, which reported 85% of the patients as having received anticoagulation [4]. This lower rate may reflect the physician's lack of awareness and reluctance.

The death or dependency rate at discharge in our study was 20%, which was comparable to studies from ISCVT (18.9%) [4] and Terrazi et al (25%) [11]. We noted a death rate of 6% at discharge, which was within the range which was reported in the literature i.e. 4.3% to 15% [4, 10, 12]. In the present study, the death or dependency rate after 12 weeks of follow up showed a good outcome (mRS<3) in 82% of the patients and a poor outcome (mRS ≥3 or death) in 18% of the patients. In a study which was done by ISCVT [4], 14% of the patients had a poor outcome after 6 months of follow up and de Bruijn et al reported an independent survival (mRS<3) in 83%

of the patients and a poor outcome in 17% of the patients after 12 weeks followup [8].

In a study which was done by Benfait et al, the mortality rate at 12 weeks of follow-up was 17.7% [13] and de Bruijn et al reported a mortality rate of 10.2% [8]. In the present study, the mortality rate after 12 weeks of follow up was 8%, which was comparable to that which was seen in other studies (Table 5).

First Author and Reference No	Year Published	Total Number of patients	Died Number	Mortality rate
Einhäupl [14]	1991	71	10	14
Ameri[15]	1992	110	6	6
Barinagarrementeria [16]	1992	78	18	23
Bienfait HP [13]	1995	62	11	18
De Bruijn [8]	2001	59	6	10
Ferro [17]	2001	142	9	6
Mehraein [18]	2003	79	8	10
ISCVT [4]	2004	624	27	4
Stolz E [12]	2005	79	12	15
Azin H [19]	2008	61	9	14
Khealani BA [20]	2008	109	10	9
Kaitazi [21]	2009	22	2	9
Fischer C [22]	2010	17	2	11

[Table/Fig-5]: Comparison of the outcome of CVST in the recent case series

We have noticed that the factors which were associated with a poor prognosis in the multivariate analysis were age > 30 years ($p < 0.05$, OR=8.46), male sex ($p < 0.01$, OR= 9), coma at presentation ($p < 0.001$, OR=80), cerebral haemorrhage ($p < 0.03$, OR=24) and deep cerebral venous system thrombosis ($p < 0.01$, OR=32). Age, National Institutes of Health Stroke Scale (NIHSS) on admission, at least two seizures during the hospital treatment despite antiepileptic treatment, venous infarct and intra cerebral haemorrhage were the factors which were associated with a poor outcome in a study by Stolz et al [12]. In a study on ISCVT, age older than 37 years, male sex, any malignancy, central nervous system infection, any seizures, mental status disorders, Glasgow Coma Score (GCS) <9 at admission, intra cerebral haemorrhage and deep venous system thrombosis were the factors which were associated with a poor outcome [4]. Coma and intra cerebral haemorrhage were the factors which were associated with a poor prognosis in a study by de Bruijn et al [8].

The prognosis of CVST was better than that which was reported previously. A subgroup (12%) of clinically identifiable CVST patients was at an increased risk of bad outcome. These high risk patients may benefit from more aggressive therapeutic interventions.

CONCLUSION

CVST is an uncommon cause of stroke with extremely diverse clinical features, predisposing factors, brain imaging findings and outcome. The post partum state and infections are the most common predisposing factors. The overall prognosis of CVST is fairly good with an independent survival of 82% and a death/dependency rate of 18%.

Age older than 30 years, male sex, coma at presentation, cerebral haemorrhage and deep cerebral venous system thrombosis on CT or MRI scan brain are the prognostic factors which are associated with a poor prognosis.

SUGGESTIONS AND RECOMMENDATIONS

Identifying patients who are at a high risk for unfavourable outcomes may provide an opportunity for the development of novel therapeutic paradigms including thrombolysis (systemic versus endovascular) and early neurosurgical interventions.

We suggest that this disease be suspected in every post partum woman with neurological symptoms and we recommend the evaluation for hyper homocystinaemia and a careful search for the central venous system, ear, nose, throat infections and face and sinus infections in the setting of CVST.

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