ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 07 | July - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICAL STUDY OF ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS OF PATIENTS WITH CEREBRAL VENOUS SINUS THROMBOSIS AT A TERTIARY HOSPITAL

Internal Medicine

Dr Nandkumar Neel Senior Resident, Image Super Speciality Hospitals and Research Center, Hyderabad, India

ABSTRACT

Cerebral venous sinus thrombosis (CVST) has been diagnosed frequently ante-mortem only in recent years. This is partly due to greater awareness among physicians and neurologists, and partly to improved non-invasive imaging techniques such as magnetic resonance imaging (MRI). Present study was aimed to study etiology, clinical features, diagnosis and prognosis of patients with cerebral venous sinus thrombosis at a tertiary hospital. Present study was single-center, prospective, observational study, conducted in patients of age > 18 years, either gender, with confirmed diagnosis (based on neuroimaging) of cerebral venous sinus thrombosis. Among 30 cases, majority were from the age group of 18-30 years (50 %), mean age of the patients was 37.6 ± 9.8 years. Male to female ratio was 1:1. Most common symptoms were headache (73.33 %) followed by convulsions (46.67 %), focal deficits (46.67 %) and vomiting (43.33 %). Common Clinical signs at presentation were hemiparesis (40 %), pallor (36.67 %), papilledema (33.33 %) & cranial nerve involvement (30 %), Anemia (36.67 %), hyperhomocysteinemia (26.67 %), protein S deficiency (20 %), puerperium (13.33 %) & OCP/HRT 2 (6.67 %) were common risk factor identified. 13 cases (43.33%) had hemorrhagic infarction, followed by Non-hemorrhagic infarction (33.33%). Most common individual sinus involved was superior sagittal sinus (43.33 %) followed by left transverse sinus (36.67%) & right transverse sinus (30 %). Two patients died during hospitalization (one due to transtentorial herniation and other from myocardial infarction). Prognosis of cerebral venous sinus thrombosis (CVST) after treatment is very good in most of the cases so mortality can be decreased by early diagnosis and treatment.

KEYWORDS

cerebral venous sinus thrombosis (CVST), MRI with MRV, LMWH, oral anticoagulants

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) has been diagnosed frequently ante-mortem only in recent years. This is partly due to greater awareness among physicians and neurologists, and partly to improved non-invasive imaging techniques such as magnetic resonance imaging (MRI). CVST is a relatively rare subtype of stroke.[1,2] In young to middle-aged adults, CVST is much more common in women than men with a ratio of approximately 3:1.[3]

Among many causes of cerebral venous sinus thrombosis recorded in the literature,[4] even with extensive investigation no cause is identified in 20 – 25% of the cases.[5] Largely inherited prothrombotic tendencies such as factor V Leiden mutations, protein S and C and antithrombin III deficiencies are an important cause, accounting for perhaps 10–15% of cases.[6] Various drugs have been implicated, including androgens, ecstasy, HRT and the oral contraceptive pill.

The diagnosis of CVST requires high index of suspicion because of its varied presentations. Neuroimaging is the corner stone in the diagnosis of cerebral venous sinus thrombosis. Imaging modalities of choice in CVST are CT scan and MRI with MR venogram.[7] Current therapeutic options for CVST treatment include anti-thrombotic therapy with un-fractionated heparin, low-molecular-weight heparins (LMWH), oral anticoagulants, intravenous thrombolysis, local thrombolysis by selective sinus catheterization and a combination of thrombolysis and anticoagulation in addition to symptomatic therapy.[8] Present study was aimed to study etiology, clinical features, diagnosis and prognosis of patients with cerebral venous sinus thrombosis at a tertiary hospital.

MATERIAL AND METHODS

Present study was single-center, prospective, observational study, conducted in department of general medicine, at Image Super Speciality Hospitals and Research Canter, Hyderabad, India. Study duration was of 1 year (January 2012 to December 2012). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients of age > 18 years, either gender, with confirmed diagnosis (based on neuroimaging) of cerebral venous sinus thrombosis, willing to participate in present study

Exclusion criteria

- Patients suspected to have Cerebral venous sinus thrombosis were evaluated & diagnosed as condition other than CVST.
- Patients with Arterial infarcts
- Patients lost to follow-up, had taken discharge against medical advice

Study was explained to patients/relatives in local language & written consent was taken for participation & study. All patients underwent collection of data such as demographic details, history, clinical examination findings, various laboratory, radiological investigations & all details were noted in case record proforma. All patients underwent detailed haematological & biochemical investigations such as complete blood count, erythrocyte sedimentation rate, basic blood biochemistry including random blood sugar, liver function tests, serum creatinine, blood urea nitrogen, serum electrolytes, prothrombin time, activated partial thromboplastin time. Special workup for hypercoagulable states including serum homocysteine, antithrombin III, protein c, protein s and anticardiolipin antibody, factor V Leiden mutation, lupus anticoagulant and other relevant investigations were done whenever required. Cerebral venous sinus thrombosis was confirmed by CT scan or conventional MRI or MR Venogram.

Treatment was given as per standard treatment protocol of institute & patients were discharged after stabilisation along with proper drug treatment, instructions for future care. Discharged patients were followed up for a period of 6 months. During follow up, data regarding disability (according to modified Rankin Scale [mRS]), death, recurrent symptomatic sinus thrombosis (new symptoms with new thrombus on repeated venogram or MRI), other thrombotic events, seizures, headaches requiring bed rest or hospital admission were recorded.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS

In present study, among 30 cases of cerebral venous sinus thrombosis, majority were from the age group of 18-30 years (50 %), mean age of the patients was 37.6 ± 9.8 years. Male to female ratio was 1:1. The mean age of female patients was 36.06 ± 17.62 years, whereas that of males was 39.14 ± 20.12 years. 4 (13.33%) patients belong to puerperal group.

Table 1- General characteristics

	No. of patients	Percentage
Age groups (in years)		
18 – 30	15	50
31 – 40	6	20
41 – 50	3	10
51 – 60	1	3.33
61 -70	3	10
71 – 80	2	6.67

Mean age (years)	37.6 ± 9.8	
Gender		
Male	15	50
Female	15	50
Type of CVST		
Non-puerperal	26	86.67
Puerperal	04	13.33

In the present study, 16 cases (53.33%) of CVST had subacute presentation, followed by 10 cases (33.33%) with acute presentation. 18 patients (60%) were conscious and 9 cases (30%) were drowsy at the time of presentation. Most common symptoms were headache (73.33 %) followed by convulsions (46.67 %), focal deficits (46.67 %) and vomiting (43.33 %). Common Clinical signs at presentation were hemiparesis (40 %), pallor (36.67 %), papilledema (33.33 %) & cranial nerve involvement (30 %),

Table 2- Clinical features

	No. of patients	Percentage
Onset		
Acute	10	33.33
Sub-acute	16	53.33
Chronic	04	13.33
Level of consciousness at the time of presentation		
Conscious	18	60
Drowsy	9	30
Stuporous	2	6.67
Comatose	1	3.33
Symptoms at presentation		
Headache	22	73.33
Convulsions	14	46.67
Focal deficit	14	46.67
Vomiting	13	43.33
Altered sensorium	11	36.67
Fever	4	13.33
Generalized weakness	2	6.67
Diplopia	2	6.67
Clinical signs at presentation		
Hemiparesis	12	40
Pallor	11	36.67
Papilledema	10	33.33
Cranial nerve involvement	9	30
Dysphasia	3	6.67

8 patients were subjected to CSF analysis whenever there was suspicion of meningitis, out of which 7 were normal and pleocytosis seen in one patient.

Table 3: CSF analysis

CSF analysis	Number of patients (n=8)	Percent (%)
Normal	7	87.5
Pleocytosis	1	12.5

Anemia (36.67 %), hyperhomocysteinemia (26.67 %), protein S deficiency (20 %), puerperium (13.33 %) & OCP/HRT 2 (6.67 %) were common risk factor identified in study. In male patients hyperhomocysteinemia (33.33 %), anemia (13.33 %) & protein s deficiency (20 %) were common risk factor identified, while among females, anemia (60 %), hyperhomocysteinemia (20 %), protein S deficiency (20 %), puerperium (26.67 %) & OCP/HRT (13.33 %) were common risk factor identified. No cause could be identified in 26.67% of male patients & 13.33% of female patients.

Table 4: Risk factors or causes identified in males

Risk factor*	Male (%)	Female (%)	Total (%)
Anemia	2 (13.33 %)	9 (60 %)	11 (36.67 %)
Hyperhomocysteinemia	5 (33.33 %)	3 (20 %)	8 (26.67 %)
Protein S deficiency	3 (20 %)	3 (20 %)	6 (20 %)
Puerperium		4 (26.67 %)	4 (13.33 %)
OCP/HRT		2 (13.33 %)	2 (6.67 %)
Protein C deficiency	1 (6.67 %)		1 (3.33 %)
APLA syndrome	1 (6.67 %)		1 (3.33 %)
Sec polycythemia	1 (6.67 %)		1 (3.33 %)
Malignancy	1 (6.67 %)		1 (3.33 %)
SLE		1 (6.67 %)	1 (3.33 %)
HIV		1 (6.67 %)	1 (3.33 %)
No cause found	4 (26.67 %)	2 (13.33 %)	6 (20 %)

*Multiple risk factors per patient identified

In the present study, 13 cases (43.33%) had hemorrhagic infarction, followed by Non-hemorrhagic infarction comprising 10 cases (33.33%).

Table 5: CT and MRI findings

Finding	Number of patients (n)	Percent (%)
Hemorrhagic Infarction	13	43.33
Non-Hemorrhagic Infarction	10	33.33
CE	9	30
CS	4	13.33

In the present study, the most common individual sinus involved (Magnetic resonance venogram findings) was superior sagittal sinus (43.33 %) followed by left transverse sinus (36.67%) & right transverse sinus (30 %).

Table 6: Sinus Involvement

Sinus involved	No. of patients(n)	Percent (%)
SSS	13	43.33
LTS	11	36.67
RTS	9	30
LSiS	5	16.67
RSiS	4	13.33
StS	4	13.33
DCV	3	10
SCV	2	6.67
ISS	1	3.33

All the 30 patients were given anticoagulation, initially with subcutaneous LMWH in 27 cases(90%) and intravenous unfractionated heparin infusion in 3 cases(10%), later on changed over to oral anticoagulants. In one patient mechanical thrombectomy with intra sinus tissue plasminogen activator installation was done. 4 patients(13.33%) required decompressive craniotomy, out of which one patient died. Additional treatments included antiepileptics in 19 patients(63.33%) and antiedema measures in 20 patients(70%). Mean hospital stay was 13.9 days in the present study (range 4 - 42).

Table 7: Treatment received

Treatment received	No. of patients (n)	Percent (%)
Anticoagulants		
· Subcutaneous LMWH	27	90
· Intravenous unfractionated heparin infusion	9	30
Interventions		
· Decompressive craniotomy	4	13.33
· Mechanical thrombectomy with intra sinus tissue plasminogen activator installation	1	3.33
Other		
· Antiepileptics	19	63.33
· Antiedema measures	20	66.67

Modified Rankin Scale score at discharge was: 0 (in ten patients), 1 (eight), 2 (six), 3 (two), 4 (one) and 5 (one). Out of the 28 survived patients, 19 (67.86%) had complete recovery, while 6 patients had residual hemiparesis, 1 had diplopia, 1 had dysphasia and 1 had persistent headache at the time of discharge. During the follow up period 3 patients had seizure recurrence while no one had recurrent CVST or thrombosis at other sites. Two patients died during hospitalization (one due to transtentorial herniation and other from myocardial infarction).

Table 8: Outcome at discharge, 3 months and 6 months

Modified Rankin Scale	At discharge (n=30)		3 months (n=28)		6 months (n=28)	
	No of cases	(%)	No of cases	(%)	No of cases	(%)
0	10	33.33	19	73.08	20	86.96
1	8	26.67	3	11.54	3	11.54
2	6	20	3	11.54	3	11.54

3	2	6.67	2	6.67	1	3.33
4	1	3.33	1	3.33	1	3.33
5	1	3.33	0	0	0	0
Death	2	6.67				

DISCUSSION

One of the greatest advances in the field of CVST is the change in outcome and prognosis of the disease throughout the years. It may be helpful in the acute stage to identify those patients who are likely to have a poor outcome, as this provides useful prognostic information for relatives and possibly influence the use of more invasive treatment.[9] In early series of cerebral venous thrombosis (largely diagnosed by angiography) and largely related to sepsis, mortality was 30–50%. Recent studies have shown a mortality rate closer to 10%.[10]

Comparing the age group involved, 20-40 years was the commonest age group involved in study by Mehta SR et al.,[11] (77.8 %) and Ameri et al.,[2] (61%), present study also showed similar findings with 56.67% in the same age group (20-40). Mean age of onset in present study was 37.6 years which is comparable with Strolz et al.[12] (42.8 years)

Male to female ratio in various studies revealed, Mehta SR et al.,[11] (1:1.4), Daif et al.,[13] (1:1), Bousser et al.,[14] (1.24:1). In the present study, M:F::1:1. The present study is comparable to Daif et al.[13] (1:1). Mehta SR et al.,[11] (1:1.4) study showed more prevalence in females may be due to use of oral contraceptive, post puerperial period

Bousser et al.,[14] had arbitrarily defined three main modes of onset based on the time elapsed between the appearance of the first symptom and the date of entry in hospital : acute as <48 hours, subacute as longer than 48 hours but less than one month and chronic as > one month. As compared to Bousser et al.,[14] Daif et al.,[13] In Indian scenario subacute presentation is more common and chronic presentation is least, whereas in New York acute and chronic Presentation is more common might be depending on severity of the disease

Headache was the most common symptom in the present study accounting for 73.3% of patients. The present study is comparable with most other studies like Bousser et al.,[14] (74 %), Mehta SR et al.,[11] (77.8 %) and Strolz et al.,[12](73.4 %).

The manifestations that indicate the cerebral cortical involvement are convulsions and paralysis; at times seizures are heralding symptoms and should arouse the suspicion of diagnosis. In the present study, 46.67% of cases had convulsions while in study by Kumar et al.,[15] (67%) & Strolz et al.,[12] (39.2 %) incidence of convulsions varied, indicate that cortical vein involvement is more common in the India as compare to USA. Whereas subcortical involvement is more common in USA and Saudi Arabia.

The frequency of involvement of different cerebral sinuses in the present study is comparable to that of Ferro et al.,[16] and Bousser et al.,[14] While Study by Daif et al.,[13] from Saudi Arabia, Strozl et al.,[12] from USA, Ferro et al.,[16] showed greater involvement of superior sagittal sinus. It indicates regional variation in venous sinus involvement might be due to genetic factor or anatomical variation.

Predisposing underlying factors can be identified in up to 80% of patients of CVST.[17] In the present study no risk factor could be identified in only 8 patients (26.67%) similar to other studies. Anemia and puerperium were the most common risk factors identified in females, whereas hyperhomocysteinemia and protein S deficiency were the most common risk factors in males. Only two of the fifteen female patients were on OCP or HRT at the time of presentation which was far less as compared to western data.[18]

Treatment of CVST ranges from observation to anticoagulation.[19] In our study all the 30 patients were treated with anticoagulants; the different routes of administration reflect uncertainty of opinions among neurologists[20] as to what type of heparin to be used. In the past, CVST had been associated with a dismal prognosis and high mortality rate, reaching 30–50%.[21] A meta-analysis of 19 studies conducted by Dentali et al.[22] showed that the mortality rate during the peri hospitalization period was about 5.6%, while at the end of the follow-up period, this percentage increased to 9.4%.

In the present study, the mean hospital stay was 13.9 days with 67.86% of the patients having complete recovery at the time of discharge. The mortality in our study is 6.67% which is comparable with Ameri et al.,[2] and Mehta et al.,[11] with 5.45% and 4.44% respectively. Most common cause of mortality is delayed diagnosis due to lack of high index of suspicious and CSVT have similar presentation as stroke. But as prognosis after treatment is very good in most of the cases so mortality can be decreased by early diagnosis and treatment.

Occasionally, patients with cryptogenic CVST later manifest symptoms of an underlying disease. The outcome of CVST is therefore generally favorable, and aggressive and potentially dangerous therapeutic interventions should be confined to those patients who deteriorate rapidly despite heparin or who demonstrate poor prognostic indicators.

CONCLUSION

Cerebral venous sinus thrombosis (CVST) is not an uncommon condition, clinical presentation is extremely varied and symptoms may evolve over hours to few weeks. Neuroimaging by MRI with MRV is the current diagnostic modality of choice. Management with unfractionated heparin or LMWH and oral anticoagulants is appropriate. Surgical decompression is helpful in the case of continuing deterioration, inspite of maximum medical management. Prognosis after treatment is very good in most of the cases so mortality can be decreased by early diagnosis and treatment.

Conflict of Interest: None to declare
Source of funding: Nil

REFERENCES:

1. Stam J,"Thrombosis of the cerebral veins and sinuses". N. Engl. J. Med. 352 (17): 1791–8.2005
2. eVeber G, Andrew M, Adams C, et al. (August 2001). "Cerebral sinovenous thrombosis in children". N. Engl. J. Med. 345 (6): 417–23.
3. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6:162–170.
4. Bousser MG. Cerebral venous thrombosis: nothing, heparin or local thrombolysis. Stroke,1999. 30:481–3.
5. Ameri A, Bousser MG. Cerebral venous thrombosis. Neurol Clin, 1992. 10:87– 111.
6. Deschiens M, Conard J, Horellou M, Ameri A, Preter M, Chedu F. Coagulation studies, factor V Leiden and anticardiolipin antibodies in 40 cases of cerebral venous sinus thrombosis. Stroke1996; 27:1724–30.
7. Wang AM. MRA of venous sinus thrombosis. Clin Neurosci 1997;4:158-64.
8. Nagaraja D, Sarma GR. Treatment of cerebral sinus/venous thrombosis. Neurol India 2002;50:114
9. Dentali F, Crowther M, Ageno W. Thrombophilic abnormalities, oral contraceptives, and risk of cerebral vein thrombosis: a meta-analysis. Blood. 2006;107:2766 –2773.
10. Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F (2005). "Cerebral vein and dural sinus thrombosis in elderly patients". Stroke 36 (9): 1927–32
11. Mehta SR, Varadarajulu R, Gupta A, Kumaravelu S. In: Joshi SR, Sainani GS, Joshi VR, Anand P, Mynadkar, Rao M et al., editors. Abstracts of 59th Annual Conference of API 2004 Jan 18-21, Hyderabad. JAPI 2003; 51:1196.
12. Strolz 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; 107(2):99-107.
13. Daif A, Awada A, al-Rajeh S, et al. (1 July 1995). "Cerebral venous thrombosis in adults. A study of 40 cases from Saudi Arabia". Stroke 26 (7): 1193–5.
14. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6:162–170.
15. Kumar S, Alexander M, Gnanamuthu C. Clinical presentation and outcome of postpartum cerebral venous thrombosis. In: Annals of Indn Acad of Neurol 2004; 7:448-9.
16. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F, for the 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;35:664-670.
17. Bousser MG, Russell RR. Cerebral Venous Thrombosis. London: WB Saunders, 1997.
18. Martinelli I, Battaglioli T, Pedotti P, Cattaneo M, Mannucci PM (2003) hyperhomocysteinemia in cerebral vein thrombosis. Blood 102:1363–1366
19. Stam J, de Bruijn SFTM, DeVeber G (2003) Anticoagulation for cerebral sinus thrombosis [Cochrane Review]. The Cochrane Library, Issue 2. Update Software Oxford, pp. 1–10
20. Masuhr F, Mehraein S, Einhaupl K (2004) Cerebral venous and sinus thrombosis. J Neurol 251:11–23
21. Nagpal RD. Dural sinus and cerebral venous thrombosis. Neurosurg Rev1983; 6:155–60.
22. Dentali F, Crowther M, Ageno W. Thrombophilic abnormalities, oral contraceptives, and risk of cerebral vein thrombosis: a meta-analysis. Blood. 2006;107:2766 –2773.