Original Research Paper

Volume-8 | Issue-12 | December-2018 | PRINT ISSN No 2249-555X

Neurology

THROMBOPHILIA PROFILE IN CEREBRAL VENOUS SINUS THOMBOSIS: A STUDY FROM EASTERN INDIA

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ABSTRACT

Background: Cerebral venous sinus thrombosis (CVST) is the formation of blood clot in the dural venous and/or sinuses, which drain blood from the brain. It is one of the commonest causes of stroke in young. In most cases it hypercoagulable factors are responsible for it.

Materials & methods: prospective observational hospital based study in the department of Neurology, S.C.B. Medical College & Hospital, Cuttack, odisha from October 2015 to September 2017. Those patients with diagnosis of CVST with magnetic resonance imaging and venogram confirmation with thrombophilia profile were included in the study. Thrombophilia assay was done. They were treated with recent guidelines. All the data were analyzed according to spss software version 20.0.

Results: Total 24 patients did the profile. Most common age group was 21-40 yrs. Protein S was the most common factor. Transverse sinus was the most common sinus. Multifactorial thrombofilia patients were more resistant to therapy.

Conclusion: All the CVST patients must be exposed to thrombophilia profile assay. It will not only help treatment of the disease but also it will help in prognosticate the outcome. In our area protein S deficiency is the most common factor abnormality. Further large studies are needed to obtain further knowledge about the factors and their clinicoradiological correlation.

KEYWORDS : CVST, Thrombophilia, protein S, Transverse sinus

INTRODUCTION:

Cerebral venous sinus thrombosis (CVST) is the formation of blood clot in the dural venous and/or sinuses, which drain blood from the brain[1]. The exact incidence varies place to place as well as studies to study. Broadly it is documented with estimated 3-4 cases per million annually in adults[1]. But the incidence is quite higher in children amounting to 7 cases per million annually[2]. Slight preponderance in females is probably due to specific causes such as oral contraceptives, pregnancy and puerperium[3]. This preponderance of females did not exist before the era of the oral contraceptive pills[3]. There is no reliable data on racial or geographical distribution but researches done in India on CVST claim that this disease is more common in underdeveloped countries of Asia than the western world[4]. The most widely studied risk factors for CVST include the prothrombotic conditions. Resistance to activated protein-C is mainly caused by the presence of the factor V Leiden gene mutation, which is a common inherited thrombophilic disorder. Hyperhomocysteinemia is a risk factor for deep vein thrombosis (DVT) and stroke but has not been clearly associated with an increased risk of CVST. Pregnancy and the puerperium are common causes of transient prothrombotic states. Approx. 2% of pregnancy-associated strokes are attributable to CVST. The frequency of CVST in the puerperium is estimated at 12 cases per 100 000 deliveries, only slightly lower than puerperal arterial stroke[5]. During pregnancy and for 6 to 8 weeks after birth, women are at increased risk of venous thromboembolic events[6]. The objective of this study was to identify the thrombotic factor commonly responsible for CVST in our hospital and compare it with other parameters.

MATERIALS AND METHODS:

It was a prospective observational hospital based study in the department of Neurology, S.C.B. Medical College & Hospital, Cuttack, odisha from October 2015 to September 2017.

Inclusion criteria-

- Patients with diagnosis of cerebral venous sinus thrombosis (CVST), confirmed by imaging of brain with MRI/MRV scan of brain.
- Patients who had done the thrombophilia profile testing after hospitalization.

Exclusion criteria:

- Patients who were clinically diagnosed as having CVST, but had normal imaging of brain (i.e. MRI/MRV scan of brain– normal).
- Patients who were not admitted to in patient department of neurology.
- Patients who didn't give consent for the study.
- Patients who denied doing the thrombophilia assay.

Consent-

Patients were included in the study after obtaining informed written consent. They were explained regarding inclusion in the study, with their mother tongue. All study related information was anonymized, kept confidential and used only for addressing the study objectives.

We included eligible participants qualifying the criteria. They were evaluated according to the epidemiological and clinical parameters. All data were tabulated in a prestructured format. Thrombophilia profile was done in a standard lab after collection of 2 ml blood with all aseptic procedure. MRI/MRV was done by 1.5 tesla MRI on day 2 of hospitalization. Treatment was done according to recent EAN guidelines. The study data was managed in MS Excel spreadsheet. Categorical data were expressed as number and percentage. Continuous data were expressed as number, mean and standard deviation depending on the distribution. Statistical significance was tested at 5% using the SPSS version 20.0. Ethical approval was obtained from institutional ethics committee.

RESULTS:

- Total 24 patients did thrombophilia assay. (n=24)
- Out of 24 patients 14 were female and 10 were male which reveals female to male ratio was 1.4:1.
- Most common age group of presentation was 21-40 years and average age was 31 year.
- Headache was the most common presentation which was seen in 20 /24 patients (83.3%).
- Papillodema was the most common finding in the group.(75%)

- **Table-1 Distribution Of Different Thrombophilia Factor Abnormality (n=24)**

Factor assay	Number of patient	% among the patients with thrombophilia assay (n=24)
Protein C deficiency	2	8.4
Protein S deficiency	4	16.7
Hyperhomocystinemia	3	12.5
Factor V mutation analysis	2	8.4

While assessing various type of coagulation factor abnormality, protein s deficiency was found to be most common (in 4 patients).

Isolated protein-S deficiency was found in only 1 patient & other 3 patient had multiple factor deficiency. Increased serum homocystein level was found in 3 patients. Protein C deficiency and Factor V mutation (heterozygous) each were found in 2 patients.

- **TABLE -2 THROMBOPHILIA ASSAY: (n=24)**

Thrombophilia testing	Number of number of patient
Protein S def.	1
Hyperhomocystinemia	2
Protein C & S deficiency	1
Factor V mutation(heterozygous)	1
Protein C & S deficiency with Factor V mutation	1
Hyperhomocystinemia +protein C & S def	1
Normal assay	17

- Total 7(29.2%) patient had 1 or more factor abnormality. About 70.8% patients who were tested for thrombophilia were found to have no abnormality.
- Radiologically parietal lobe involvement was found to be commonest, in 8 patients (33.3%). Transverse sinus was the most common sinus involved in 19(79.1%) patients.
- The multifactorial thrombophilics were more resistant to thrombolytic treatment. At 3 months in repeat MRV they were having persistence of the thrombus.

DISCUSSIONS:

Cerebral venous sinus thrombosis is a condition characterized by thrombosis of intracranial veins and sinuses. It may results in parenchymal damage and rise in intracranial pressure, but it can also present with signs & symptoms even without any radiological observable parenchyma damage. Radiological hallmark of this condition is the presence of thrombus in the intracranial sinuses and/or veins with or without associated haemorrhagic infarction, oedema & features of intracranial hypertension.

In the present series, patients were female to male ratio was 1.4:1. It has been suggested that the incidence of CVST was higher in females. Most of the earlier case series from India have reported a higher proportion of women suffering from CVST than men[7]. Similar trends are observed in this study. The cause can be attributed to high incidence of some major risk factors which are indigenous to the female sex only (Like pregnancy, purperium, use of oc pills). However due to lack of large population based study, potential predominance female patients among the CVST cases could not be negated with the present study.

More than half (63.5%) of the patients of CVST in the present series, were in the 3rd & 4th decade of their life (15/24). The mean age of the patients was 31.85 years (with SD12.29 years) similar to earlier studies from India.[7] Mean age of the patients was also found to be 31.3 years in the recent series from Nizam's Institute Venous Stroke Registry [NIVSR], the largest hospital based prospective study in India[8] It confirms the postulation that CVST is a disease affecting primarily young adults & the age of presentation has not changed significantly from the earlier studies.

Headache was present in 83.3% patients in present series and was the most common symptom. Out of them, 71.2% of patients had holocranial headache and 11.5% of patient had hemicranial headacahe. This is similar to the earlier observations as well as the recent ones like, NIVSR Cohort, where 88.3% patients had headache as the presenting complaint of CVST.[8] Out of total 24 patient 75% (18/24)) patients had papilledema at presentation. This finding is similar to various previous studies[9].

Thrombophillia assay was done in all 24 patients of this study group. Among these patients 29.2% patients had 1 or more coagulation factor abnormality. About 70.8% patients who were tested for thrombophilia were found to have no factor abnormality /deficiency. While assessing individual type of coagulation factor abnormality, protein-S deficiency was found to be most common, in 4 patients. Isolated protein-s deficiency was found in only 1 patient other 3 patient had multiple factor deficiency. Hyperhomocystinemia, Heterozygous Factor V mutation was found in 3 and 2 patients respectively. The most common risk factor identified for CVST throughout the world is often a prothrombotic condition [9]. In the ISCVT cohort, a prothrombotic condition was found in 34% of all patients, and a genetic prothrombotic condition was found in 22% of all patients. [10] Almost all the large series from the developed countries have a large proportion of patients having a prothrombotic condition as a risk factor. However, most of the earlier published studies from India did not have information regarding these inherited prothrombotic states probably due to lack of laboratory facilities to conduct these tests. Recently, in a cohort 612 consecutive patients from various hospitals of Bombay, Pai et al.[11] observed that 18% of the patients were positive for the thrombophilia markers, with protein C deficiency being the most common thrombophilia marker followed by a deficiency of protein S, FVL mutation, and AT deficiency. This study had a similar percentage of patients with a hereditary prothrombotic condition, when compared to that reported from developed countries. Similarly, Narayan et al., also reported 12.3% patients having a genetic prothrombotic condition as a risk factor for CVST.[11] The proportion of CVT patients with a prothrombotic condition in India is also probably similar to that of Western countries and has been probably under-reported in the earlier studies & the present series confirms this higher incidence of hereditary prothrombotic condition. However in the present study protein S deficiency & hyperhomocystinemia were more prevalent. This could possibly be due to regional variation of thrombophilic condition .As this is a relatively small study, further analysis is needed in large number of subjects to assess the prevalence of various factor deficiency in our population in this region.

Transverse sinus was the most common sinus involved both in isolated and combination in the present series. In most of the previous studies, Superior sagittal sinus was the most frequent sinus involved either alone or in combination with other sinus.[8] This might be because of small study sample as well as geographical variations. The multifactorial thrombophilic patients were more resistant to the anticoagulant therapy. In repeat MRV scan they were having persistence of clot in venous sinuses. Those patients were 3 in number. They were having multiple thrombophilia profiles. But they had both protein c and protein s deficiencies were common. It was associated with other factors like hyperhomocystinemia or factor V deficiency (table-2).

CONCLUSION:

The probability of CVST should be kept in mind in every patient having acute or subacute headache with or without visual changes after ruling out common etiological factors. Sensitivity of suspicion should be more when the patient possesses any risk factor. Thrombophilia profile is a must for every CVST patient. Protein S was most common factor in our study but it may differ in other geographical areas. Treatment guidelines and clinical improvement depend upon the profile.

Conflicts of interest: nil
Funding : nil

REFERENCES

1. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6:162–170.
2. Dlamini N, Billinghurst L, Kirkham FJ (2010) Cerebral venous sinus (sinovenous) thrombosis in children. NeurosurgClin N Am 21: 511-527.
3. Ferro JM, Lopes MG, Rosas MJ, Femo 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 2002; 13:272-278.
4. Pillai LV, Ambike DP, Nirhale S, Husainy S M, Pataskar S. Cerebral venous thrombosis: An experience with anticoagulation with low molecular weight heparin. Indian J Crit Care Med 2005;9:14-8
5. Ventura P, Pabinger I, Grafenhofer H, Kyrle PA, Quehenberger P, Mannhalter C, Lechner K, Kaider A Temporary increase in the risk for recurrence during pregnancy in women with a history of venous thromboembolism. Blood. 2002;100:1060–1062.
6. Jaigobin C, Silver FL Stroke and pregnancy. Stroke. 2000; 31:2948–2951.
7. Nagaraja D, Taly AB, Puerperal venous sinus thrombosis in India. In: Sinha KK ed. Progress in clinical neurosciences, Ranchi, NSI, Publications 1989;5:165-177.
8. Narayan D, Kaul S, Ravishankar K, Suryaprabha T, Bandaru VC, 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;60:154-9.
9. Biousse V, Ameri A, Bousser MG: Isolated intracranial hypertension as the only sign of cerebral venous thrombosis. Neurology 1999; 53:1537.
10. Ferro JM, Canhão P, Stam J, Bousser MG, 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; 35:664–670.
11. Pai N, Ghosh K, Shetty S. Hereditary thrombophilia in cerebral venous thrombosis: A study from India. Blood Coagul Fibrinolysis 2013;24:540-3.