Section: Neurology

Original Research Article

RETROSPECTIVE ANALYSIS OF ETIOLOGIC ASSOCIATIONS IN PATIENTS OF CEREBRAL VENOUS THROMBOSIS: A HOSPITAL BASED STUDY

Ajit Prasad Mishra[1], Srikant Kumar Sahoo[2], Srimant Pattanik[1], Nilesh Wagh[3], Hareen Choudhary Veerapaneni[3], Chandraprava Mishra[4]

[1]Associate Professor, Department of Neurology, IMS & SUM Hospital, Odisha, India.
[2]Professor, Department of Neurology, IMS & SUM Hospital, Odisha, India.
[3]Resident student, Department of Neurology, IMS & SUM Hospital, Odisha, India.
[4]Assistant Professor, Department of Pathology, S.C.B. Medical College, Odisha, India.

Received : 04/08/2023
Received in revised form : 08/09/2023
Accepted : 22/09/2023

Keywords:
Risk factors, cerebral venous thrombosis, thrombophilia assay.

Corresponding Author:
Dr. ChandrapravaMishra,
Email: chandraprava51@gmail.com

DOI: 10.47009/jamp.2023.5.5.268

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (5); 1356-1359

Abstract

Background: Cerebral venous thrombosis (CVT) is the formation of blood clot within the venous system of brain and its pathological consequences. This has an estimated incidence of 3-4 cases per million populations among adults annually with a slight female preponderance. **Materials and Methods:** This is a retrospective analysis of medical records of patients with diagnosis of cerebral venous thrombosis to determine various etiological associations. **Result:** Medical records total 64 patients of CVT were analyzed. Female to male ratio was 1.3:1. Majority of the patients were in their twenties or thirties, with headache as the most common symptom at presentation. Known risk factors, prior to etiological work up were present in 27 (42.2%) patients. Most common association among the predisposing conditions was use of OC pill in 10 (15.6 %) patients. Twenty-two patients (34.4%) had one or more thrombophilic disorder. **Conclusion:** Risk factors identification is very important in CVT patients. Though thrombophilia assay is not very well studied in our population, but it should be done for every CVT patient as it helps in treatment and secondary prevention of the condition.

INTRODUCTION

Cerebral venous thrombosis (CVT) is an abnormal coagulation of blood within the veins or dural sinuses of brain. This causes impaired venous drainage of the blood, causing hemorrhagic infarcts, brain edema and raised intracranial pressure.[1] The incidence of cerebral venous thrombosis varies from region to region, also amongst different studies. Broadly it has an estimated annual incidence of 3-4 cases per million population among adults1 with a slight female preponderance and about 7 cases per million among the children.[2]

Information on racial or geographical distribution of CVT was not reliably available but previous researches from India indicate a higher prevalence of CVT in our country country.[3] Commonly observed risk factors for CVT are prothrombotic conditions like anti thrombin III deficiency, protein C/S deficiency, factor V Leiden gene mutation etc. Transient prothrombotic conditions like pregnancy, puerperium and dehydration are also commonly found in CVT patients.[4,5] Objective of this study was to determine the distribution of various risk factors among the CVT patients in our hospital.

MATERIALS AND METHODS

This is a retrospective study performed in the department of neurology of IMS & SUM hospital, Bhubaneswar. Medical records of all patients with clinical diagnosis of cerebral venous thrombosis during the five year period from May 2018 to April 2022 were analyzed. Out of total 103 patients, 64 patients who had confirmation of CVT diagnosis by CT venogram or MR venogram of brain and had undergone thrombophilia assay were included in the study. Other 39 patients who were incompletely evaluated or in whom detailed history preceding onset of symptoms were not available, were excluded from the study.

All patients' information was anonymized, kept confidential. The data obtained was tabulated in a pre-structured data booklet and managed using MS Excel spreadsheet. This was used only to obtain the study objectives.

RESULTS

Out of total 64 patients 36 were female and 28 were male. The female to male ratio was 1.3:1. Majority

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of the patients were in their twenties or thirties, with headache as the most common symptom at presentation, (in 81.3% of patients). On evaluation of etiological association of various conditions, 16 patients of CVT were found to be anemic. Microcytic hypo-chromic feature s/o iron deficiency was seen in 12 patients; four patients had hemolytic features. Subsequently they were diagnosed to have sickle cell trait on hemoglobin electrophoresis. Among other patients with anemia, severe anemia was found in only four patients. Moderate to mild anemia was seen rest of the eight patients. No other etiologic association, except mild anemia could be found in 10 patients.

OC pill use as an association was the next most common acquired condition, found in 10 CVT patients. Hereditary thrombophilia was found in 22 patients. Distributions of various etiological associations are shown in [Table 1].

Known risk factors, prior to etiological work up were present in 27 (42.2%) patients. Most common association among the predisposing conditions was use of OC pill in 10 (15.6 %) patients. Two patients were in 3rd trimester of pregnancy and one patient was in 1st week of postpartum period. Previous history of deep venous thrombosis was found in two patients and both of them found to have antithrombin-III deficiency subsequently. At time of presentation, no previously known risk factor could be found in 37 (57.8 %) patients. Among the 64 patient who were evaluated in the study 12 (18.7%) patients had an exposure to a triggering event (events/health issues that are plausible to be responsible for initiation of the CVT) within one week prior to initiation of CVT symptom. Among them, local suppuration was found in four patients with one having sinusitis and other three having chronic suppurative otitis media (CSOM). Two patients had head and neck injury preceding the onset of CVT. One patient had severe exertion and dehydration due to prolonged physical work in the field. Another patient developed dehydration following loose motion and vomiting during a febrile illness. Two patients developed CVT in association of meningitis. Various plausible risk factors and triggering conditions that were found in this series were described in [Table 2].

Twenty two patients (34.4%) had one or more thrombophilic disorder. Normal thrombophilia assay was found in 65.6 % patients. Majority of patients had multiple hereditary thrombophilia with protein S deficiency being most common. Distribution of different thrombophilia abnormality is shown in [Table 3].

Table 1: Etiologic Association

Etiologic association	Number of patient
OC pill	8
OC pill+ Hyperhomocystinemia	1
OC pill+ CNS infection (meningitis)	1
CNS infection (meningitis)	1
Sickle cell trait and Anemia	4
Systemic infection with severe cachexia (military TB)	1
Local suppuration (csom/sinusitis)	4
Unspecified febrile illness with gastroenteritis with dehydration	1
Pregnancy with antithrombin III deficiency	2
Puerperium	1
Chronic hepatitis B antithrombin III deficiency	1
Sturge –weber syndrome with Protien C def.	1
DM withProtien C +Protein S def	3
DM with Antiphopholipid Ab Syndrome	1
DM with factor V heterozygous mutation	1
Hyperhomocystinemia + dehydration	1
Hyperhomocystinemia with Protein S def	2
protein-c def .+ proteins s def.+ hyperhomocystinemia	2
Blunt head & neck trauma +protein c def.+protein-s def	2
Hyperhomocystinemia + protein-s def .+ factor V heterozygous mutation	1
Antiphopholipid Ab Syndrome	2
Anemia with antithrombin III deficiency	2
Anemia	10
No etiologic association	11

Table 2: Risk Factors/Conditions

Risk factors/conditions	Number of patient
Head & neck trauma	2 (3.1 %)
Local suppuration (CSOM, Sinusitis)	4 (6.2%)
Severe exertion/Dehydration	2 (3.1%)
Meningitis	2 (3.1%)
Unspecified febrile illness	2 (3.1%)
H/o DVT	2 (3.1%)
OC pill use	10 (15.6%)
Pregnancy & Puerperium	3 (4.7%)
No prior risk factor	37 (57.8 %)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 3: Thrombophilia Factor Assay

Factor assay	Number of patient
Protein S deficiency	10 (15.6%)
Protein C deficiency	8 (12.5%)
Antithrombin III deficiency	5 (7.8%)
Hyperhomocystinemia	5 (7.8%)
Factor V mutation analysis	2 (3.1%)
Antiphopholipid Ab Syndrome	3 (4.7%)

DISCUSSION

The present series of CVT observed a female to male ratio was 1.3:1, showing a little higher proportion of female amongst the CVT patients. Various previous studies from India and abroad reported a higher percentage of female patients suffering from CVT compared to males [6]. Greater incidence of certain risk factors, like pregnancy, purperium, OC pills usage exclusive to female sex may be reason of it.

In the present study, known risk factors,[7] were present in 42.2% patients at time of presentation prior to etiological work up. Most common association was the use of OC pill in 15.6 % patients, which included one patient who also recently had medical termination of pregnancy. Conventional risk factors like meningitis (3.1%) local suppuration (ex. csom, sinusitis) (6.2%), dehydration (3.1%), past h/o venous thrombosis (3.1%), Pregnancy & puerperium (4.7%) were also found in various patients. In addition to these known risk factors, head and neck trauma (3.1%) and systemic febrile illness (3.1%) were also seen. On analyzing various etiological associations with respect to CVT anemia was found to be the single most common association in 18.7% of patients in the present series. Though iron deficiency anemia is described as risk factor for CVT, higher incidence of anemia in this series may also be due to disproportionate high prevalence of iron efficiency anemia in the study population.[8,9]

Among these CVT patients, 34.4% had one or more thrombophilic abnormality. Most common abnormality was found to be Protein- S deficiency (in 15.6% patients) followed by protein-C deficiency (in 12.5% of patients). Other abnormalities like, Hyperhomocystinemia (7.8 %) patients, Antithrombin III deficiency (7.8%) and Factor V mutation (3.1%) was also observed. Antiphopholipid Ab Syndrome as an etiological association was seen in 4.7% of patients. A thrombophilic abnormality is often identified as one of the commonest risk factor for CVT in different regions. [10,11] In the ISCVT cohort, Prothrombotic conditions were identified in 34% of patients, and a genetic thrombophilic disorder was diagnosed in 22% of the patients.[12] Though previous studies from western countries had a large proportion of patients with prothrombotic conditions, most of the earlier data from India lacked information regarding this. In a study involving 612 patients from western india, 18% of Patients were found to have thrombophilia abnormalities. The protein C deficiency was the commonest followed by the deficiency of protein S, anti thrombin III and FVL mutation.[13] The present study had patients with a hereditary prothrombotic conditions in a relatively higher proportion. As this is a retrospective analysis, exact timing of thrombophilic assays could not identified. This may explain a relatively higher percentage of patients with thrombophilic factor abnormality due to early testing among the patients. It's possible that the proportion of CVT patients with a prothrombotic condition is similar between India and Western countries. This has been probably under-estimated in the previous series due to lower testing of thrombophillic factors earlier days.

In this study protein C deficiency and protein S deficiency were more commonly found. Probably this was due to genetic variations of thrombophilic conditions in different populations and less number of study subjects. Analysis of a large number of subjects over a wide geographic region is needed to determine the true prevalence of various hereditary thrombophilic abnormalities in our population.

CONCLUSION

Identification of risk factors in CVT patients greatly helps in treatment and secondary prevention of the condition. The importance of thrombophilia assay is not very well studied in our population, but thrombophilia assay should be done for every CVT patient. Though this is a relatively small study, but it confirms the greater incidence of hereditary thrombophilic conditions in the CVT patients in our region.

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. 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 CritCare Med 2005;9:14-8.
4. 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 inwomen with a history of venous thromboembolism. Blood. 2002;100:1060–1062.
5. Jaigobin C, Silver FL Stroke and pregnancy. Stroke. 2000; 31:2948–2951.
6. 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.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

7. Caso V., Agnelli G.,Paciaroni M., Handbook on Cerebral Venous Thrombosis , In Bogousslavsky, Montreux J., Series Editor ,Frontiers of Neurology and Neuroscience,Vol. 23,karger,2008,23-54.
8. Stolz E, Valdueza JM, Grebe M, Schlachetzki F, Schmitt E, Madlener K, Rahimi A, Kempkes- Matthes B, Blaes F, Gerriets T, Kaps M: Anemia as a risk factor for cerebral venous thrombosis?An old hypothesis revisited: results of a prospective study. J Neurol2007;254:729–734.
9. Yilma, H., Sedlander, E., Rimal, R.N. et al. The reduction in anemia through normative innovations (RANI) project: study protocol for a cluster randomized controlled trial in Odisha, India. BMC Public Health 20, 203 (2020). https://doi.org/10.1186/s12889-020-8271-2.
10. 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 sinusvenous thrombosis: Insights from Nizam's Institute Venous Stroke Registry, Hyderabad(India). Neurol India 2012;60:154-9.
11. Biousse V, Ameri A, Bousser MG: Isolated intracranial hypertension as the only sign ofcerebral venous thrombosis. Neurology 1999; 53:1537.
12. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F ISCVTInvestigators.Prognosis of cerebral vein and dural sinus thrombosis: results of theInternational Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke.2004; 35:664–670.
13. Pai N, Ghosh K, Shetty S. Hereditary thrombophilia in cerebral venous thrombosis: Astudy from India. Blood Coagul Fibrinolysis 2013;24:540-3.

ISSN (O): 2687-5365; ISSN (P): 2753-6556