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ORIGINAL ARTICLE

CLINICAL RELEVANCE, ETIOLOGY AND IMAGING CHARACTERISTICS OF CEREBRAL VENOUS SINUS THROMBOSIS AT A TERTIARY CARE HOSPITAL IN BANGLADESH

MD. RASHEDUL ISLAM[1], AMINUR RAHMAN[2], TANBIN RAHMAN[3], MOHAMMAD SAKHAWAT HOSSEN KHAN[4], DILRUBA ALAM[5], RUMANA HABIB[6]

Abstract

Background: *Cerebral sinus thrombus (CVST) is a rare form of stroke often affects young people with diverse clinical, etiological and radiological presentation. The aim of the study was to evaluate clinical relevance, etiologies, and imaging characteristics of CVST in Bangladesh.* ***Methods:*** *A prospective, observational study was done at a tertiary care hospital with patients recruited in the period of January 2021 to January 2023. 38 patients with clinical and radiological features suggestive of cerebral venous sinus thrombosis (CVST) were studied with thorough clinical evaluation and comprehensive work up.* ***Results:*** *The mean age of presentation was 28.42 years with female predominance (n = 24). Headache was the most common presenting symptoms (92%, n = 35) followed by vomiting (52%, n = 20). Hemi paresis (38%; n = 14) was the most common clinical sign followed by cranial nerve palsy (26%, n = 10). 31% of the patients (n=12) had provoked CVST among those the most common cause was found to be pregnancy/puerperium in 58% (n = 7 patients) followed by OCP which were 25% (n = 3). 69 % of the patients (n=26) had unprovoked CVST among those the most common cause was found to be prothrombotic conditions in 85% (n = 22 patients) followed by idiopathic which were 15% (n = 4). In magnetic resonance imaging venography (MRV), 74% of patients (n = 28) had thrombosis of transverse sinus, 53% of patients (n = 20) had thrombosis of the sigmoid sinus and 42% patients (n = 16) of patients had saggital sinus thrombosis.*

Conclusion: *Clinical presentation is variable, etiology must be determined, and diagnostic method of choice is MRV. Headache was most the common clinical presentation and the most common etiological factor is puerperium. Provoked CVST is more common than unprovoked CVST and transverse sinus thrombosis frequently involved.*

Key words: *Clinical relevance, Cerebral venous sinus thrombosis, Hemorrhagic infarct, imaging characteristics*

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1. Associate Professor, Department of Neurology, BIRDEM General Hospital, Dhaka, Bangladesh.
2. Assistant Professor Dept. of Neurology, Sir Salimullah medical college , Mitford, Dhaka, Bangladesh.
3. Assistant Professor (Medicine), Anwer khan modern medical college hospital, Dhaka, Bangladesh.
4. Registrar, Department of Neurology, BIRDEM General Hospital, Dhaka, Bangladesh.
5. Assistant Professor, Department of Neurology, BIRDEM General Hospital, Dhaka, Bangladesh.
6. Associate professor, Department of Neurology, BIRDEM General Hospital, Dhaka, Bangladesh.

Correspondence: Md. Rashedul Islam, Associate Professor, Department of Neurology, Room-1420, 13th Floor, BIRDEM General Hospital, Shahbag, Dhaka-1000, Dhaka, Bangladesh. Email: rashed2k2001@yahoo.com

Introduction:

Cerebral sinus thrombus (CVST) is a rare form of stroke that accounts for 0.5-1% of all strokes and often affects young people[1]. Overall CVST has an incidence of 0.22– 1.32/100,000/year.[4] It occurs more frequently in young adults in contrast to arterial stroke and three times more common in females than in males.[2, 3] The basic pathology of CVST is thrombosis of cerebral veins and the commonest site of origin is thought to be the junction of cerebral veins and larger sinuses.[4] Once a thrombus is formed in the cerebral or cortical veins, it can propagate and occlude large draining venous sinuses. This causes physiological back pressure in the venous system, leading to cerebral oedema and occasionally cerebral infarction and haemorrhage.[5, 6]

The variability of clinical pictures complicates the clinical diagnosis of CVST and sometimes leads to a high rate of suspicion in the diagnosis. In addition, there may be regional differences in the incidence of risk factors and clinical manifestations.[7] The clinical presentation of CVST is variable and categorized like this: symptoms and signs of raised intracranial pressure (ICP), a focal brain lesion, or both a focal lesion and raised ICP. Onset is also variable and up to 40% of patients can present acutely with a stroke-like syndrome within 48 h of symptom onset. [5] Headache is the most common symptom and is present in <"90% of cases; in 25% of patients, it is reported as the only symptom .[7] Given a lower incidence of headache in arterial stroke (25–30%), [8] the presence of severe headache in the context of stroke-like symptoms can raise suspicion of CVST. Seizures are also a presentation in CVST compared with arterial stroke (40% vs 6%). Focal neurological symptoms and signs are common, such as motor weakness (present in up to 40% of patients). [5] Cerebral venous sinus thrombosis can be provoked or unprovoked and numerous risk factors are reported in individual patients. Up to 90% of patients with CVST have at least one risk factor for venous thromboembolism (VTE), and thrombophilias (genetic or acquired) are detected in more than 30% of patients.[5] Female-specific risk factors are more important in younger age groups (ie oestrogen containing contraceptives, pregnancy and puerperium). [6]

Neuroimaging is important to the diagnosis of CVST and working with radiologists to identify the most appropriate imaging techniques is important. There are certain characteristics of parenchymal lesions that are suggestive of CVST, including bilateral or parasagittal lesions, lesions crossing arterial territories, and juxtacortical lesions.[9] Magnetic Resonance Imaging (MRI) brain with Magnetic Resonance Venography (MRV) is the current diagnostic modality of choice with very high sensitivity and specificity.[110] Management of CVST is focused on timely diagnosis and treatment. The current therapeutic options for CVST includes antithrombotic treatment with heparin overlapping with oral anticoagulants, thrombolysis (intravenous/local thrombolysis by selective sinus catheterization) and a combination of thrombolysis and anticoagulation.[11] Evaluation for an underlying pro-coagulant state may be rewarding for further prevention with long term anti coagulation. Outcome of CVST is a bit unpredictable, it is not unusual to see dramatic recovery in deeply comatose patient and, sudden worsening in conscious patients due to extension of thrombosis. [12] Early diagnosis and appropriate treatment of CVST is essential, as it may prevent morbidity and can be life saving.

On the contrary to the disease burden, there is a scarcity of data on CVST in Bangladesh. We therefore attempted to fill the gap to understand CVST in a Bangladeshi setting, by conducting this study at our referral center. Our aim was to see the clinical profile, etiological factors and imaging charecteristics CVST patients who were admitted at a tertiary care hospital.

Methods:

We conducted a single-center, prospective, descriptive study was carried out in the neurology department of BIRDEM General Hospital, Dhaka, Bangladesh. Study protocol was approved by the institutional ethics committee and only patients/next of kin who gave a written informed consent were included in the study. The study design was a prospective, observational study with patients recruited in the period of January 2021 to January 2023. A successive of 38 admitted patients in neurology department were included in the study initially based on the clinical profile of raised intracranial pressure and seizures with or without neurological deficits.

The diagnosis of CVST was made using established diagnostic criteria [13], which include (i) a clinical hypothesis of CVST (headache, focal neurological deficit and cranial hypertension) (ii) supported by neuroimaging showing a "delta sign" on cranial computed tomography (CT) scan and magnetic resonance imaging (MRI) or MR venography showing cerebral sinus or venous occlusion. Cranial hypertension was clinically diagnosed by neuroimaging. After diagnosis, all consecutive patients (aged 20–60 years) with confirmed CVST were

included in the study after obtaining written informed consent. Patients with clinical symptoms suggestive of arterial stroke or primary cerebral hemorrhage, aged 18 to 60 years, with sinusitis, intracranial space occupying lesions, metabolic encephalopathy, visual impairment due to optic nerve papilledema diagnosed by fundoscopy, or unenhanced CT showing the arterial region, infarction or hemorrhage were excluded from the study.

Neuroimaging was performed by experienced radiologists who were unaware of the patients' clinical signs and symptoms to avoid influencing the diagnosis. Magnetic resonance imaging (MRI) was performed on a 1.5 T machine (Philips). The MR scan protocol included an axial Fluid Attenuated Inversion Recovery (FLAIR), axial and coronal T2W, T1 3D sagittal. The location, extent and nature of abnormalities were recorded. Magnetic resonance venography (MRV) was used in both coronal and axial planes in the lower saturation band to eliminate signals from arterial structures.

All patients underwent complete blood count, routine blood biochemistry and coagulation profile, and routine laboratory tests for hypercoagulable conditions including protein C, protein S, antithrombin III, factor V Leiden, homocysteine, phospholipid bodies (APLA). Other studies were performed when necessary. Genetic tests were not performed due to financial constraints.

The data thus collected was entered into Microsoft Excel work sheets. Frequencies for the clinical features, etiology and radiological findings were analyzed. Statistical analysis was done via SPSS version 25 (SPSS Inc. Chicago, IL USA). Discrete variables were listed as counts or percentages.

Results:

A total of 38 patients were included in this study, 24 (63%) were females and 14 (37%) were males. The mean age of presentation was 28.42 years with female predominance (n = 24). Headache was most the common presenting symptoms (92%, n = 35) followed by vomiting (52%, n = 20). Most common pattern of headache was diffuse throbbing type (51%) followed by dull aching headache (22%). Hemi paresis (38%; n = 14) was the most common clinical sign followed by cranial nerve palsy (26%, n = 10). Among the cranial nerve palsy cases, upper Motor Neuron (UMN) seventh nerve palsy was present in 6 cases and bilateral sixth nerve paresis in 4 patients.

Table-I

Clinical profile of cerebral venous sinus thrombosis in study group.

Symptoms and signs	No. of patients	Percentage
Headache	35	92
Vomiting	20	52
Seizure	8	21
Altered Sensorium	12	32
Hemiparesis	14	38
Fever	4	11
Papilledema	7	18
Cranial nerve involvement	10	26
Dysarthria/aphasia	3	8

In Table II an etiological point of view, 12/38 (31%) had clear clinical triggers and were considered provoked CVT in this study. In this subset, pregnancy/ puerperium 7/12(58%), OCP use 3/12 (25%) and para infectious 2/12 (17%), were identified as risk factors for provoking CVT. The breakdown of para infectious CVST included mastoiditis (1 patient), bacterial meningitis (1 patient). In the other subset of unprovoked CVST 26/38 (69%) where no clinical triggers were evident, a standard procoagulant workup was done. In 22 (85%) of these cases a prothrombotic state could be identified.

Table-II

Etiologic profile of cerebral venous thrombosis in the study

Risk factors	No. of patients	Percentage
Provoked (12/38)		
Parainfectious	2	17
Pregnanacy/puerperium	7	58
OCP use	3	25
Unprovoked (26/38)		
Procoagulant conditions	22	8515
Idiopathic	4	

In Table: III This included Protein C deficiency in 9/ 22 (41%), Protein S deficiency in 7/22 (32%), APLA in 2/22 (9%) and Anti thrombin III deficiency 1/22 (5%). Some patients had combined pro-thrombotic states like combined Protein C & S deficiency in 3 cases. In the remaining 4/26 (15%) no clear clinical or lab abnormality could be identified and these were considered Idiopathic subset in this study. They may

have factor VIII elevation or genetic prothrombotic states like FVL (Factor V Leiden) or MTHFR (methylenetetrahydrofolate reductase) which was not tested for in this study.

Table III

Pro-coagulant conditions identified in unprovoked CVST

Procoagulant conditions (n = 22)	No. of patients	Percentage
Protein C deficiency	9	41
Protein S deficiency	7	32
APLA panel	2	9
At III deficiency	1	5
Combined Prot C & S Def	3	14

There were various MRI findings of CVST patients in which hemorrhagic infracts were 53%, and 18(47%) cases had dural and cortical CVST without parenchymal lesions as shown in Fig.-1.

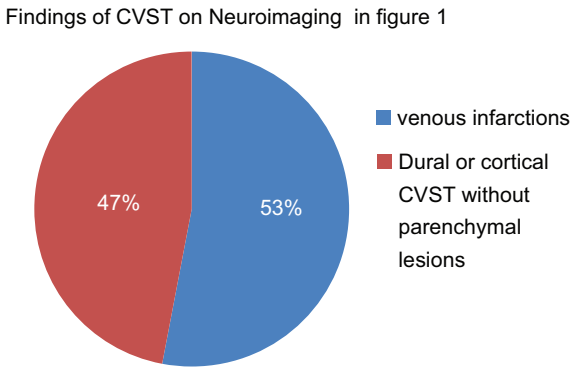

Fig.-1: *Findings of CVST on MRI of Brain.*

In Table IV 74% of patients (n = 28) had thrombosis of transverse sinus, 53% of patients (n = 20) had thrombosis of the saggital sinus thrombosis and 42% patients (n = 16) of patients had sigmoid sinus. 40% of patients (n = 15) had multiple sinus involvement.

Table IV

Sinuses involved on MRV in the study group.

Sinus involved	No. of patients	Percentage
Transverse sinus (TS)	28	74
Superior sagittal sinus (SSS)	20	53
Sigmoid sinus (SS)	16	42
Straight sinus	2	5
Cortical veins	1	3
Deep veins	1	3
Multiple sinus involvement	15	40

Discussion:

Cerebral venous sinus thrombosis, unlike arterial stroke, often occurs in young individuals.[14] Due to diverse clinical presentation, it is often a diagnostic challenge for the clinicians. Modern neuro-imaging techniques and diagnostic laboratory investigations are providing precious information about risk factors and clinical profile of CVST. In this study, we tried to highlight and compare its variable clinical presentations, etiological factors and neuro-imaging findings with other studies.

Comparing the age group involved, 20–40 years was the commonest age group involved in various studies with mean age of onset being 35 years. The present study also showed similar finding with mean age of onset being 28.42 years. Our study showed female preponderance (F: M – 1.7:1), in contrast to some other studies.[15,16] Headache was the most common symptom in the present study accounting for 92% of patients. Most common pattern of headache was diffuse throbbing type (56%) followed by dull aching headache (26%). Seizures are far more frequently seen in CVST than in arterial stroke. At times seizures are heralding symptoms in CVST and should arouse the suspicion of the diagnosis. In our study, 21% of cases had seizures which are comparable with another study.[12] The types of the seizures observed in the patients were generalized tonic-clonic (68%), focal with or without dyscognitive features (22%) and focal with secondary generalization (10%). 32% patients had altered level of consciousness at presentation, which is comparable with Vidyasagar S et al.[17] and Dhadke VN et al.[18] In this study, 11% patients had fever at the onset which is similar to findings of another study.[18]

Prothrombotic conditions are the most common risk factor identified for unprovoked CVST in published literature throughout the world. In the International study on Cerebral Venous Thrombosis (ISCVT) cohort[5], 34% patients had prothrombotic conditions, and 22% had underlying genetic prothrombotic states. However, we didn't find earlier published studies from Bangladesh that have information regarding these prothrombotic conditions due to paucity of laboratory data. Recently Pai et al.,[12] and Zhou L.-X et al.,[14] reported thrombophilia as a risk factor for CVST in 18% and 12.3% patients respectively. In our study 22/26 (85%) of the unprovoked CVST patients had predisposing thrombophilic conditions. Another study stated that, 29/36 (81%) of the unprovoked CVST of their patients had underlying thrombophilic condition.[19] This included Protein C deficiency in 9/22 (41%), Protein S deficiency in 7/22 (32%), APLA in

2/22 (9%) and Anti thrombin III deficiency 1/22 (5%). Majority of cases of CVST as recorded in published literature, have multifactorial etiology, which suggests that pro-thrombotic workup should be extensive. However, this is not always possible to do due to financial issues. In the present study, 12/38 (31%) had clear clinical triggers and were considered provoked CVST. In this subset, pregnancy/ puerperium 7/12(58%) were identified as risk factors for provoking CVST. Another study stated that, puerperal group consists of 4/15 (26%).[18] Among the cases of unprovoked CVT In 15% (4/26) of cases we were unable to find any cause even after procoagulant workup, this constituted Idiopathic cases in our study. They may be harboring some form of genetic thrombophillia like FVL or MTHFR mutation or Factor VIII elevation, but we could not test due to financial constraints.

In the present study transverse sinus was most frequently involved (28/38) 74% followed by superior sagittal sinus in (20/38) 53%, sigmoid sinus in (16/ 38) 42%, Straight sinus in (2/38) 5%, cortical veins alone in (1/38) 3% and deep veins in (1/38) 3% which is comparable with another study.[1] Another study done in India showed that, transverse sinus was most frequently involved (40/54) 74% followed by superior sagittal sinus in (29/54) 52%, sigmoid sinus in (27/ 54) 50%, Straight sinus in (4/54) 7%, cortical veins alone in (2/54) 4% and deep veins in (1/50) 2% in their study. [19] In the present study, 20 cases (53%) had venous infarctions on MRI brain, out of which 12 cases (60%) were hemorrhagic infarctions and 8 cases (40%) were non-hemorrhagic infarctions in a venous distribution. The remaining 18 (47%) cases had only dural or cortical CVST without parenchymal lesions. Similar observations were noted in other studies.[20]

Conclusion:

CVST is an under recognized cause of headache and stroke in young patients. Our study suggested that an essential clinical feature of CVST is the new onset of headache. The most common etiological factor is puerperium . Provoked CVST is more common than unprovoked CVST. It was also observed that the most common sinus involved in transverse sinus. So early diagnosis of CVST will help in planning for the appropriate management of the patients.

Limitations of the study:

This study was conducted in a single center. A complete thrombophilia evaluation could not be performed in every patient due to financial constraints and genetic study was not done.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of of BIRDEM General Hospital, Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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