Clinical Profile, Risk Factors and Outcome of the Patient with Cerebral Venous Sinus Thrombosis at 3 Months: Prospective Cohort Study in a Tertiary Care Hospital

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Abstract:

Background: *Cerebral venous sinus thrombosis (CVST) one of the important type of venous stroke. With the advent of the newer imaging technique, it is now increasingly diagnosed in our country. There are limited studies regarding venous stroke specially about its outcome in Bangladesh. So, we conducted the study to observe the clinical profile, risk factors and outcome of the patient with cerebral venous sinus thrombosis at 3-month in a tertiary care hospital.*

Methods: *This Prospective cohort study was carried out in the Department of Neurology, Dhaka Medical College Hospital during January 2022 to December 2023. The patients suffering from cerebral venous sinus thrombosis confirmed by imaging were included in this study. The outcome was assessed with mRS score.*

Results: *We included 58 patients with venous stroke, among them about 2/3rd were female. The mean age (SD) of the was 36.46(13.56). Most of the patients were between 20 and 40 years.*

The most common clinical presentations were headache 54(93%), vomiting 36(62%) and seizure 21 (36.2%). The focal neurologic deficit was present in 17(29%) and papilledema in 33(56.89%) of the patients. The risk factors for CVST identified in the study included CNS infections 22 (41%), then pregnancy and puerperium 8(62%), intake of OCP and other hormonal preparation 6(90%), COVID -19 infection and post vaccination (6.90%), and idiopathic 34(48%). D-dimer was elevated in half of the patients. The commonest sinuses involve were transverse sinus 31(65.51%), and superior sagittal sinus 13 (43.10%). Multiple sinuses involvement was present in more than 2/3rd cases. The mean (SD)hospital stay was 12.4 (3.8) days. At 3-month 44(76%) had mRS 2 score and only 10% patient died. Mortality was higher among males, who had multiple sinus involvement and multiple comorbid conditions.

Conclusion: *CVST largely affect the young female, mostly present with headache vomiting and seizure. Generally, the outcome is good with conventional treatment.*

Keywords: *Cerebral venous sinus thrombosis; Headache; Puerperium; MR Venogram; OCP; Seizure.*

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Introduction

Thrombosis of the cerebral venous sinus (CVST) is a form of venous stroke, usually affecting young individuals.[1] Despite advances in the recognition of CVST in recent years, diagnosis and management can be difficult because of the diversity of clinical profile, underlying risk factors and the absence of a uniform treatment approach. CVST represents 0.5% to 3% of all strokes.[2,3]

In recent years, cerebral venous sinus thrombosis (CVST) has been diagnosed substantially more frequently than in the past

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due to the expanded use of noninvasive brain imaging methods. However, the actual incidence of CVST is most likely even higher. Many cases remain unrecognized due to the high variability of their clinical presentation and the possible absence of any symptoms.

CVST can be caused by prothrombotic states (congenital or acquired) such as deficiencies in anticoagulation-promoting protein, use of oral contraceptives, pregnancy, dehydration, trauma, inflammatory diseases, infections and haematological conditions. The presenting clinical profiles of CVST quite puzzling. CVST may be encountered not only by neurologists and neurosurgeons but also by emergency physicians, oncologists, ophthalmologists, hematologist's, obstetricians, family practitioners due to diversity of causes and presenting scenarios.[4]

Clinical findings in CVST usually fall into two major categories, depending on the mechanism of neurological dysfunction: Those that are related to increased intracranial pressure attributable to impaired drainage and those related to focal brain injury from venous ischemia/infarction or hemorrhage. The clinical presentation of CVST can be with focal neurological deficits and/or seizures, headache, papilledema, and intracranial hypertension and coma and may lead to death.[5] Headache is one of the common presenting symptoms in around 70%-90% of patients. Still others can present with diffuse encephalopathy, painful ophthalmoplegia, or status epilepticus.[5] Acute symptomatic seizures are reported in about 35%-50% and around 76% in peripartum period in 29% of the patients, seizure is the presenting sign, and 59% of them had a generalized seizure.[6]

The diagnosis of CVST is typically based on clinical suspicion and imaging confirmation. Various laboratory studies along with MRI and MRV are necessary for stablishing a diagnosis. Recently, CVST is diagnosed early and with increased frequency due to easier access to magnetic resonance imaging (MRI). MRI with magnetic resonance venogram (MRV) has very high sensitivity and specificity and has become the modality of choice.[7]

CVST treatment options include treatment of the identified risk factors; (antithrombotic therapy; and symptomatic treatment of intracranial hypertension, seizures, and other complications including secondary infections, physiotherapy, and supportive measures. Antithrombotic therapy are anticoagulation with unfractionated heparin or low molecular weight heparin, even the patient have intracranial hemorrhage.[8]

CVST may cause serious neurological syndromes and the mortality rate ranges 5.5-30%.[9]

The prognosis of CVST patients has improved over the last decades due to increase in diagnosis of CVST and improved care and early treatment. Mortality in the West is now below 5%. About 80% of the patients make a full independent recovery. Mortality is mainly related to fatal brain herniation, caused by large hemispheric hemorrhagic infarcts.[10] Other deaths are related to metabolic derangements, status epilepticus, infections, aspiration pneumonia, and rarely to pulmonary embolism.[11]

The optimal duration of oral anticoagulation after the acute phase is unclear. Oral anticoagulation may be given for 3 months if CVST was secondary to a transient risk factor; for 6–12 months in patients with idiopathic CVST and in those with mild hereditary thrombophilia, and indefinite anticoagulation should be considered in patients with chronic major risk factors for thrombosis or recurrent venous thromboembolism of CVST.[12,13,14]

Overall, the patient with CVST have a favorable outcome. Most of the patient with CVST survive without physical disability, but some symptoms negatively affect quality of life. The outcome of CVST depends upon various factors. Women with younger age, having no comorbidity and mRS < 3 with better outcome compared with male patients with CVST.[15] Poor prognostic factors are advance age, active cancer, decrease

level of consciousness, and intracerebellar hemorrhage.[16] The were limited studies about CVST in Bangladesh. So, the base line information about its presentation, risk factors and outcome is largely unknown among Bangladeshi population.

So, present study has been designed to identify the clinical presentations, risk factors, and outcome of patients with CVST.

Materials and Methods

It was a prospective cohort study conducted in the department of Neurology, Dhaka Medical College Hospital. Ethical approval was obtained from the Dhaka Medical College ethical review board prior to the study. Informed written consent was obtained from all the study participants.

Study participants:

The study included patients aged more than 18 years, both sexes and confirmed cerebral venous sinus thrombosis by MRV or DSA. Patients with previous venous stroke, concomitant ischemic stroke, and prior disability due to other causes were excluded from the study. We included every consecutive patient, fulfilling the inclusion and exclusion criteria.

Study procedure:

We collected the data by interviewing the patients or their attendant and recorded the data in the case record form. The history of previous disease and personal habits as well as demographic, vascular risk factor, biochemical data and CT or MRI findings was recorded. In all patients, neurological assessment was conducted by the consultant Neurologist. Cerebral venous sinus thrombosis was diagnosed on the basis of positive lesions on CT head, MRI of brain, MRV or DSA of brain. The patient was treated by the respective Department according to standard guideline. Th-e outcome determinants was mortality and morbidity, recurrence, as measured using the modified Rankin Scale (mRS) at discharge, at end of 1 month and at the end of 3 months. A mRS of 3-6 will be considered as poor outcome and mRS of 0-2 as good outcome. In cases where the patient was failed to visit the hospital, a telephonic mRS was recorded. The telephone guideline was validated.

Statistical analysis

The data was analyzed with Statistical Package for Social Scientists-26 (IBM SPSS-26). The qualitative data was expressed with n (%). The quantitative data were test for the normality. The data were found normally distributed and were expressed with mean (SD). The groups were compared with chi-square test if qualitative variable and unpaired t-test in case of quantitative variable. The predictors for mortality were determined with logistic regression test and OR was expressed with 95% CI. The p value <0.05 was considered as significant.

Results

During the study period, total 100 patients was admitted to this institute with CVST. Among the 58 included in this study as per inclusion criteria. the majority of our patients (67.24%) were female. The mean (SD) age of the participants was 36.46(13.56). The most common symptoms were headache in 54 patients (93.10%) and most common clinical sign was papilledema (33 patients,56.89%; Table 1). Disease onset was acute in 46 patients (79%), but was subacute or chronic in in 8 (13.8%) and four (6.9%) respectively. Clinical presentations of CVST were variable. Most of the patient with CVST presented with headache 54 (93.10%). Headache was variable in characteristics ranges from mild to moderate, dull or throbbing in nature. A few patients presented with sudden severe thunderclap like headache (10%). Other presentation included were vomiting (62.07%), seizure (36.21%), focal neurological deficit (29.32%). (Table II).

The most common risk factors for CVST in this study were infection (22.41%), pregnancy and puerperium (8.62%), post vaccination (6.90%), OCP and other hormonal preparation (6.90%), malignancy (5.17%) and idiopathic (39.66%). The most common clinical sign in this study was papilledema (56.8%). (Table III).

Table I

Demographic characteristics of patient with cerebral venous sinus thrombosis:

Variable	Results	Percentage
Age(mean±SD)	36.46±13.56	
Sex		
Female	39	67.24
Male	19	32.76
Hospital stay (mean±SD)	14.46±4.05	
Educational status		
Primary	22	37.93
Secondary	21	36.21
Graduate	15	25.86
Occupation		
Homemaker	33	56.90
Students	8	13.80
Others	17	29.31
Comorbidity		
No	46	79.31
DM	8	13.79
HTN	4	6.90

Table II

Clinical presentation of patients with cerebral venous sinus thrombosis:

Symptoms and signs	Number	Percentage
Headache	54	93.10
Vomiting	36	62.07
Seizure	21	36.21
Focal neurological deficit	17	29.32
Papilledema	33	56.89

Table III

Risk factors of patients with cerebral venous sinus thrombosis:

Name	Frequency	Percentage
Infection	13	22.41
Pregnancy and puerperium	5	8.62
Post vaccination	4	6.90
Drugs	4	6.90
Malignancy	3	5.17
Idiopathic	23	39.66
Others	6	10.34

In MRV most commonly involved sinuses are transverse sinus 31 (65.51%), superior sagittal sinus 13(43.10%), sigmoid sinus 7 (12%) and multiple sinus involvement was present in 46 cases (79.31%), and single sinus involvement in only 12 cases (20.69%) (Table IV)

Table IV

Sinus involvement in patient with cerebral venous sinus thrombosis:

Name of sinus	Number	Percentage
Transverse sinus	38	65.51
Superior sagittal sinus	25	43.10
Sigmoid sinus	7	12
Deep venous sinus	2	3.40
cavernous sinus	1	1.70
Multiple sinus involvement	46	79.31
Single sinus involvement	12	20.69

Table V

causes of CVST by different infection

Infection	
Abdominal TB	01
CSOM	02
Brain abscess	02
Bacterial meningitis	03
Encephalitis	01
Septicemia	01
Dengue encephalitis	01
Acute pancreatitis	01
Puerperal sepsis	01

Bacterial meningitis and CSOM were important cause of infection causing CVST.

Average hospital stay was 12.46+3.81 days. There was significant improvement (mRS<3) of symptoms at discharge. Multiple logistic regression analysis revealed female sex, those who are married, OCP users, event during puerperium and post vaccination had poor outcome. Those who had involvement of superior sagittal sinus and transverse sinus had poor outcome. The mortality rate in the current study was 6(10.34%) (Figure 1).

Table V

Predictors of outcome among cerebral venous sinus thrombosis:

Variable	OR (95%CI)	P-value
Age	1.184(1.007-1.391)	0.041
Sex	1.635(0.046-58.705)	0.788
Headache	0.248(0.005-20823.95)	0.810
Vomiting	0.027(0.001-0.844)	0.040
Altered consciousness	18.5(1.81-188.38)	0.009
Hemiparesis	57.283(1.580-2077.369)	0.027
Papilledema	0.241(0.054-2.938)	0.043
6th nerve palsy	1.14(0.134 – 10.54)	0.588
DM	0.89(0.81-0.98)	0.724
OCP	1.19(1.00-1.41)	0.352
Infection	0.87(0.778-0.984)	0.311
TST	1.15(1.01-1.303)	0.237
SSST	1.12(1.01-1.25)	0.513
Sigmoid sinus	1.02(0.152-6.59)	0.690
Deep venous	0.896(0.813-0.981)	0.808
Cavernous sinus	0.898(0.817-0.987)	0.900

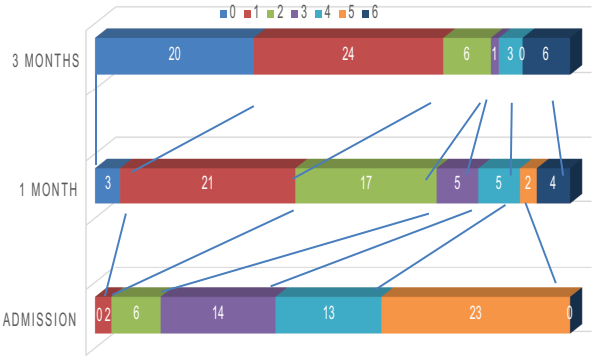

Figure 1: *Score on the modified Ranking scale at admission, end of one month and at three months:*

Discussion

In this study the majority of our patients were young female, mostly presented with headache, vomiting and seizure. Most of the patient had multiple venous sinus involvement. Transverse sinus thrombosis was the most common site of thrombosis followed by superior sagittal sinus and sigmoid sinus. Overall outcome at 3 month was good and the mortality was low.

We cannot generalize the study findings for whole Bangladesh, as population was selected from one selected hospital in Dhaka city, Outcome may differ in different treatment facilities.

Most of the patients were between 20 and 40 years. In a study by Saposnik G al 2011 most of the patients were between 25-35 years with a maximum 72 years.[2] The study by Patil et al in 2014 found that 78% of patients were younger than 50 years.[17] As in our study female preponderance was also noted in the study by Saposnik G al 2011.[2] Gender specific factors like use of OCP, pregnancy, puerperium, HRT might be responsible for such preponderance.[12]

The clinical presentation like headache, seizure, vomiting and focal signs found in this study is similar to other studies.[12,17,18]

The nature of the Headache in about one fourth of the patients was as thunderclap, was similar in De Bruijn et al.[4] Seizures were focal in one quarter of patients, in another quarter they begin as focal then generalized, and remaining half are generalized which is similar to other studies.[19]

Focal neurological deficit such as paresis, dysarthria and aphasia are due to localized damage in cerebral cortex.

In our study Papilledema was the commonest clinical finding which was present more than half of patients that matched with other studies.[20, 21] It due to raised ICP due to venous stasis.[22]

CVST has multifactorial etiology. The risk factors for developing cerebral venous sinus thrombosis are infection, pregnancy and puerperium, post vaccination, OCP and other hormonal preparation, malignancy and idiopathic.[23]

A local infection i.e. CSOM, meningitis become a strong risk factor in our study(table 5). Septic venous sinus thrombosis is rare in the anti-biotic era[24], but after the COVID pandemic we get increasing evidence of septic venous thrombosis.[25]

D-dimer was found to be raised in half of total patients in this study which is almost similar to the study. But has low sensitivity and specificity in diagnosis CVST.[26] In our study it is also not a predictor of bad outcome as well.

Neuro-imaging is the cornerstone in the diagnosis of cerebral venous sinus thrombosis. Imaging modalities of choice in CVST are CT scan and MRI of brain with MR Angiogram. CT scan may be normal in 1/3rd cases but MRI with MRV is almost 100% diagnostic.[18] In this study only more than half of patients have CT brain abnormality and 100% of patients had MRV abnormality.

All patients were treated with low molecular weight heparin (LMWH) followed by DOAC. Fifty patients (86%) stabilized and later improved. Heparin was then switched to oral anticoagulants. Average hospital stay was 12.46+3.81 days. There was significant improvement (mRS<3) of symptoms at discharge. Hemiplegia was persistent at discharge in less than 1/3rd cases.

The patients who presented with headache, vomiting, double vision, blurring of vision, had better outcome (mRS<3) whereas those who presented with seizure, altered level of consciousness and focal neurological deficit papilledema, had poor outcome (mRS>2). Multiple logistic regression analysis revealed female sex, those who are married, OCP users, event during puerperium and post vaccination had poor outcome.

The mortality rate in the current study was 6(10.34%) which was similar to that in other studies.[18] The patients who died are female and of younger age <30 years and presented with headache, repeated seizures and altered level of Consciousness and hemiparesis.

Conclusion:

CVST largely affect the young female, mostly present with headache vomiting and seizure. Generally, the outcome is good with conventional treatment.

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Conflict of interest

The authors have no conflicts of interest

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