

ORIGINAL ARTICLES

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

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Abstract:

Background: Cerebral venous sinus thrombosis (CVST) one of the cause 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 patients with Cerebral venous sinus thrombosis (CVST) at 3 month in a tertiary care hospital. **Objective:** To see the clinical profile, risk factor and outcome of the patient with cerebral venous sinus thrombosis at 3 month in a tertiary care hospital. **Methods:** This Prospective observational and non interventional descriptive study was carried out in the Department of Neurology, Neurosurgery, Gynecology and obstetric & Medicine of Dhaka Medical College Hospital during January 2022 to December 2023. The patients suffering from cerebral venous sinus thrombosis were included in this study. Age > 18 year, both male & female patients with features of cerebral venous sinus thrombosis enrolled in this study. **Results:** During the study period, total 58 patients admitted to this institute with Thrombosis of the cerebral venous sinus (CVST). Among the 58 patients about two-third were female. The mean age of the was 36.46 ± 13.56 . Most of the patients were between 20 and 40 years. The most common clinical presentations were headache which was present more than two-third of the patients, vomiting was present near half of the patient, seizure was present one-third of patients, focal neurological deficit was present one quater of patients, near half of patient suffer from visual disturbances. In this study papilloedema was the commonest clinical finding which was present more than half of patients. CVST has multifactorial. The risk factors for developing cerebral venous sinus thrombosis are infection, pregnancy and puerperium, post vaccination, Oral Contraceptive Pill and other hormonal prepration, malignancy and idiopathic. Most common risk factors among the study were infection (22.41%), then pregnancy and puerperium (8.62%), intake of Oral Contraceptive Pills and other hormonal prepration (6.90%), Covid -19 infection and post vaccination (6.90%), and no risk factors was found among (34.48%). In our study anemia was found in more than one-third of patients, D-dimer was found to be raised in half of total patients in this study. The commonest sinus involve most are transverse sinus 31(65.51%), then superior sagitta sinus 13 (43.10%), multiple sinus involvement was present in more than two-third cases and single sinus involvement in only one quater patients. Average hospital stay was 12.46 ± 3.81 days. There was significant improvement of symptoms and signs during discharge from hospital after medical treatment as evidence by (mRS > 3). The mortality rate was 10.34%. **Conclusion:** The transverse sinus thrombosis was the most common and bilateral cavernous sinus thrombosis was the uncommon affection in CVST. Mortality was more in patients who has multiple sinus involvement, male sex and had some multiple comorbid conditions.

Keywords: Cerebral venous sinus thrombosis; Headache; Magnetic Resonance Venogram; Seizure. Risk factors of CVST

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Introduction

Thrombosis of the cerebral venous sinus (CVST) is an uncommon form of 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 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 scenarios⁴.

Clinical findings in CVST usually fall into 2 major categories, depending on the mechanism of neurological dysfunction: (1) Those that are related to increased intracranial pressure attributable to impaired drainage and (2) 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 death⁵. 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 epilepticus⁵. 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 seizure⁶.

The diagnosis of CVST is typically based on clinical suspicion and imaging confirmation. Various laboratory studies along with MRI and MRV are necessary for establishing 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 choice⁷.

CVST treatment options include (1) treatment of the identified risk factors; (2) antithrombotic therapy; and (3) 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 haemorrhage⁸.

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 infarcts¹⁰. Other deaths are related to metabolic derangements, status epilepticus, infections, aspiration pneumonia, and rarely to pulmonary embolism¹¹. Author have reported unfavorable outcome (50% of modified Rankin score 4 or 5: or 42% to die) when bilateral lesions where present compare to 11% in unilateral lesions.

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 favourable 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 CVST¹⁵. Poor prognostic factors are advance age, active cancer, decrease level of consciousness, and intracerebellar haemorrhage¹⁶.

The venous strokes especially in young females of childbearing potential are under-diagnosed due to lack of knowledge. So, present study has been designed to identify the clinical presentations risk factors, and outcome of patients with CVST in neurology department in Dhaka medical college hospital.

Materials and Methods

A prospective cohort study was conducted in department of Neurology, Medicine, Neurosurgery and Gynaecology & Obstetrics DMCH. Patients with at least 18 yrs of age and cerebral venous sinus thrombosis were diagnosed by neuroimaging. Patient with confirmed CVST, gender matched, 18 yrs or older and willing to participate considered inclusion criteria of this study. Patient were excluded from the study if they had Concomitant arterial ischemic stroke, having intracerebral space-occupying lesions, hydrocephalus, ICP within normal range and Previous diagnosed case of CVST.

Ethical approval was obtained from the DMCH ethical review board prior of study. After selection of the subjects, the nature, purpose and benefit of the study was explained to each subject in details. They were encouraged for voluntary participation. Informed written consent was taken from the participants. The history of previous disease and habits as well as demographic, vascular risk factor, biochemical data and CT findings was recorded. Anthropometric measurement (height, weight) of the subjects was done and blood pressure was measured. BMI was calculated as weight (kg) / height (m)². In all patients, neurological

assessment was conducted routinely. Cerebral venous sinus thrombosis was diagnosed on the basis of positive lesions on CT head, MRI of brain, MRV scan of brain. All the information was recorded in a structured data collection sheet. The 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 will be recorded.

Statistical Analysis

All the data were compiled and sorted properly and the numerical data were analyzed statistically by using Statistical Package for Social Scientists (IBM SPSS-26). The results expressed as frequency, percentage, mean $\pm$ SD. 95% confident interval (CI) will be calculated and p value <0.05 will be considered as the level of significance.

Results

A total of 58 patients were screened for enrollment as per inclusion criteria. the majority of our patients 67.24% were female. Median age was 36 yrs (ranges years) and there is no significant difference in the median age of men and women. The most common symptoms was headache in 54 patients (93.10%) and most common clinical sign was papilloedema (33 patients, 56.89%; Table I). Disease onset was acute in 46 patients (), but was subacute or chronic in 8 () and four () respectively; there was no difference in speed of onset between men and women. Clinical presentation of CVST are variable. Most of the patient with CVST are presented with headache 54 (93.10%). Headache was variable in characteristics ranges from mild to moderate, dull or throbbing in nature. A few patients were presented with sudden severe thunderclap like headache (10%). Other presentation are vomiting (62.07%), seizure (36.21%), focal neurological deficit (29.32%). Focal deficit are more frequent in patient with thrombosis of the superficial venous system with the involvement of parasagittal cortex (Table II).

Table-I
Sociodemographic characteristics of patient with cerebral venous sinus thrombosis

Variable	Frequency (n)	Percentage
Age(mean±SD) in years	36.46±13.56	
Sex category:		
Female	39	67.24
Male	19	32.76
Hospital stay (mean±SD) in days	14.46±4.05	
Educational status:		
Primary	22	37.93
Secondary	21	36.21
Occupation		
Homemaker	33	56.90
Students	8	13.80
Comorbidity		
No	46	79.21
DM	8	13.79
HTN	4	6.90

Table-II
Clinical mainifestation 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
Papilloedema	33	56.89

The most common risk factors in this study are infection (22.41%), pregnancy and puerperium (8.62%), post vaccination (6.90%), OCP and other hormonal prepration (6.90%), malignancy (5.17%). The most common clinical sign in this study was papilloedema (56.89%).

A local infection otitis media, mastoiditis, sinusitis, meningitis accounts for 22.41%, then pregnancy and puerperium (8.62%), OCP and post vaccination was respectively 6.90%. No risk factos was found in 23 cases (Table III).

CT scan may be normal in one/third cases. 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-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

Table-IV
Site 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

Average hospital stay was 12.46+3.81 days. There was significant improvement (mRS> 3) of symptoms at discharge. The patients who presented with headache, vomiting, double vision, blurring of vision, had better outcome (mRS<2) 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. 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%) (Table V and 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
6 th nerve palsy	1.14(0.134-10.54)	0.588
Diabetes Mellitus	0.89(0.81-0.98)	0.724
Oral Contraceptive Pill	1.19(1.00-1.41)	0.352
Infection	0.87(0.778-0.984)	0.311
Transverse Sinus Thrombosis	1.15(1.01-1.303)	0.237
Superior Sagittal Sinus Thrombosis	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

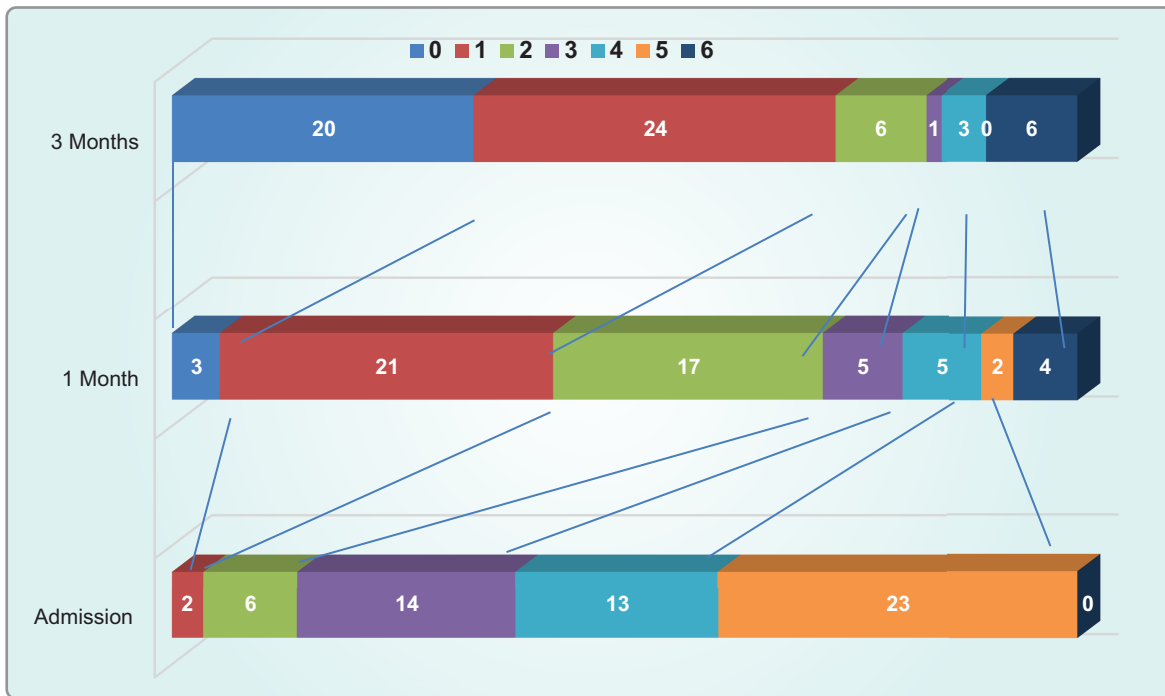


Figure 1: Score on the modified Ranking scale at admission, end of one month and at three month :

Discussion

In terms of financial, social, and health costs, stroke is one of the most common diseases in Bangladesh. Venous stroke are usually not commonly diagnosed due to lack of suspicious and availability of diagnostic modality. In this study the majority of our patients 67.24% were female. Median age was 36yrs. The most common symptoms was headache (93.10%). In 63.52% of our patients, inherited or acquired risk factors for thrombosis were detected. Transverse sinus thrombosis was the most common site of thrombosis (65.51%), followed by superior sagittal sinus and sigmoid sinus. Two third of the patients had involvement of multiple sinuses. The patients with the involvement of transverse sinus had better disability at the time of admission while the number of involved sinuses correlated worse disability. Most of the patients 36 (62.07%) had mRS >3 and at the end of 3 month most of the patient mRS < 3 (87.93%).

These study is not applicable generally, because of population was selected from one selected hospital in Dhaka city, patient age >18 yrs., some risk factors like genetic prothrombotic factors and uncommon hematological conditions were not possible to evaluate.

During the study period, total 100 patients was admitted to this institute with cvst. Among the 58 included in this study. Among them about 2/3rd were female. The mean age of the was 36.46 ±13.56. Most of the patients were between 20 and 40 years. In the study by Saposnik G al 2011 most of the patients were between 25-35 years with a maximum 72 years. The study by Patil et al in 2014 found that 78% of patients were younger than 50 years. As in our study female preponderance was also noted in the study by Saposnik G al 2011.

In this study the common clinical presentations were headache which was present more than 2/3rd of the patients, vomiting was present near half of the patient, seizure was present 1/3rd of patients, hemiparesis was present one quarter of patients, near half of patient suffer from visual disturbances which is almost similar to that in other studies (Patil et al., 2014; Yadav Kapinder et al., 2016 ; Ferro JM

et al.,2017). Headache is usually the first manifestation at onset of CVST. About 1/4th cases headache was thunderclap in nature, mimicking subarachnoid hemorrhage which was similar in De Bruijn et al.,2001. Seizure are focal in one quarter of patients, in another quarter they begin as focal then generalized, and remaining half are generalized which is similar in Dentali F 2006.

Focal neurological deficit such as paresis, dysarthria and aphasia are due to localized damage in cerebral cortex. Focal deficit are more frequent in patient with thrombosis of the superficial venous system with the involvement of parasagittal cortex.

In our study papilledema was the commonest clinical finding which was present more than half of patients that matched with the study by Gunes HN., et al 2016. Papilledema was due to

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. In our study about 1/3rd of the patient has no identifiable risk factors which was higher in other studies i.e. Yadav et al., 2016 which was due to small size population, limitation and availability of investigation. In the study by Saposnik G al 2011 intake of OCP was the commonest (66.03%) risk factor for cerebral venous sinus thrombosis.

A local infection i.e. otitis media, mastoiditis, sinusitis, meningitis become a strong risk factor in our study. In the study by Hinnell C et al the incidence of Para nasal sinus infection was 27%. Approximately 7% patient with CVST have a concomitant malignancy which was similar in Dentali F et al.,2006..During the period of Covid 19 significant number of cerebral venous sinus thrombosis found due to direct effect of Covid 19 infection and post covid vaccination.

In our study anemia was found in more than 1/3rd of patients, which is higher than that in other studies (26.7% by Jalili et al.) which is possibly due to nutritional deficiency and multiparity.

D-dimer was found to be raised in half of total patients in this study which is almost similar to the study by

Pfefferkorn et al., 2009. Elevated D-dimer levels were not predictors of poor outcome (mRS 3).

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 venogram. CT scan may be normal in 1/3rd cases but MRI with MRV is almost 100% diagnostic (Yadav et al., 2016). In this study only more than half of patients have CT brain abnormality and 100% of patients have MRV abnormality which is consistent with other studies.

In MRV most commonly involved sinuses are transverse sinus 31 (65.51%), superior sagittal sinus 13(43.10%), sigmoid sinus 7 (12%) which is almost similar to that of other studies (Gunes et al., 2016; Khealani et al., 2006). Multiple sinus involvement was present in more than 2/3rd cases and single sinus involvement in only one quarter patients. Logistic regression analysis revealed that the frequency of transverse sinus thrombosis is higher in OCP users which was also revealed in other studies (Gunes et al.

2016;Khealani et al., 2006). All patients were treated with low molecular weight heparin (LMWH) followed by DOC. 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 (23.80%) of the patients. One patient presented with impaired level of consciousness which did not improve at the time of discharge. The patients who presented with headache, vomiting, double vision, blurring of vision, had better outcome (mRS<2) 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. Those who had involvement of superior sagittal sinus and transverse sinus had poor outcome. The majority more than 2/3rd of study patients had an admission mRS score >3 whereas during discharge majority

had an mRS <1. Study by Yadav et al in 2016 found a partial and/or total recovery from illness in 42 (84%) patients. The mortality rate in the current study is 6(10.34%) which is similar to that in other studies (Yadav et al., 2016). 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

Most common risk factors for venous sinus thrombosis in this study are oral contraceptive, infection and puerperium. Outcome of the patient at discharge admitted with venous thrombosis depends on risk factors, type and number of venous sinus involvement. Only few patients were died, early diagnosis and treatment may reduce morbidity and mortality of cerebral venous sinus thrombosis.

Acknowledgments

We want to thank the patients in the study, our colleagues, and the department of Neurology, Neurosurgery, Medicine, Gynecology and obstetrics, DMCH. We acknowledge the BDMCH authorities for their support in conducting the study.

Conflicts of interest

The authors have no conflicts of interest

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