



## Clinical, Etiological and Prognostic Factors of Cerebral Venous Sinus Thrombosis in Kashmir-North India

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### Abstract

**Background:** Cerebral venous sinus thrombosis (CVST) has a variable clinical presentation making early diagnosis difficult. A number of prothrombotic states have been implicated in causation of CVST, but results are mixed.

**Aims:** The study was aimed to find out the clinical, etiological and prognostic factors of CVST in Kashmir-North India.

**Materials and Methods:** The study was carried out in a tertiary care hospital where all patients of CVST admitted between 1st August 2014 and 31<sup>st</sup> July, 2016 were included in the study. The enrolled patients were studied for their demographic profile and a 2-5ml blood sample was collected from the subjects as well. Patients were followed up for minimum period of 6 months and outcome was assessed on the basis of morbidity and mortality.

**Results:** A total of 36 patients of CVST were included in the study. The mean age of the patients was 35.5 years with highest representation (38.89%) among 31-40 years age group. Headache was present in 94.4%. 30 patients (83.3%) were alive at the end of follow-up and 6 patients died (16.6%). Among various etiological factors purperium has a maximum representation (33.33%). Out of 32 female patients in the study group, 16 (44.44%) female patients had puerperium and 06 (16.66%) had oral contraceptive as a risk factor. Unconscious with purposive movements was observed in 27.78% of the subjects. Out of 39 patients who survived, 31 cases (79.4%) had no disability symptoms, 5 patients had mild disability (13%) and 3 patients had moderate disability at six months of follow-up.

**Conclusion:** Purperium appears to be the main etiological factor and headache as the most common symptom for CVST in study population.

**Keywords:** Clinical; etiological; prognostic factors, Cerebral Venous Sinus Thrombosis; Kashmir.

### Introduction

Cerebral Venous Sinus Thrombosis (CVST) is an uncommon form of stroke, usually affecting

young individuals<sup>(1)</sup>. Due to the diversity of underlying factors and the absence of a uniform treatment approach, management and diagnosis of

patients remain a challenging task. Despite advances in the recognition of CVST in recent years, diagnosis and management can be difficult because of the diversity of underlying risk factors and the absence of a uniform treatment approach<sup>(2)</sup>. Multiple factors have been associated with CVST, but only some of them are reversible. Medical abnormalities including recent surgery, postpartum state, pro thrombin gene mutation and hyperhomocysteinemia, thrombophilia, inflammatory bowel disease, pregnancy, infection, head trauma, cancers and medications like oral contraceptives (OCPs) are some influencing conditions<sup>(3-6)</sup>.

The diagnosis of CVST is typically based on imaging confirmation and clinical suspicion<sup>(7-10)</sup>. Clinical findings in CVST usually fall into; increased intracranial pressure attributable to impaired venous drainage and focal brain injury from venous ischemia/infarction or haemorrhage<sup>(7,11,12)</sup>. When focal brain injury occurs because of venous ischemia or haemorrhage, neurological signs and symptoms referable to the affected region are often present; most common are hemiparesis and aphasia, but other cortical signs and sensory symptoms may also occur. In practice, many patients have clinical findings due to both mechanisms, either at presentation or with progression of the underlying disease.

CVST is an important diagnostic consideration in patients with headache and papilledema or diplopia (caused by sixth nerve palsy) even without other neurological focal signs suggestive of idiopathic intracranial hypertension. The headache of CVST is typically described as diffuse and often progresses in severity over days to weeks. Sometimes, headache is presented with subarachnoid haemorrhage (SAH) and a migrainous type<sup>(13)</sup>.

Magnetic resonance imaging (MRI) and/or Non-contrast computed tomography (NCCT) are the most frequently performed imaging studies for evaluation of patients with new headache, focal neurological abnormalities, seizure, or change in mental status. But NCCT may only show indirect signs of thrombosis, including diffuse brain edema

and parenchymal haemorrhage and sensitivity. NCCT in the diagnosis of CVST was previously considered rather poor as compared to MRI<sup>(5,14,15)</sup>.

Considering the above literature regarding the etiology, symptoms and diagnostic features of CVST, our aim was to characterize clinical presentations, risk factors, clinical course, and outcome of the disease in our population.

### Materials and Methods

A total of 36 patients of cerebral venous sinus thrombosis presenting in a tertiary care hospital Sheri-Kashmir Institute of Medical Sciences (SKIMS), Srinagar from 1<sup>st</sup> August 2013 to 31<sup>st</sup> July 2016 (prospective) were included in the study.

All patients aged above 18 years with one and/or more clinical features consistent with CVST like seizures, headache, papilledema, focal neurological deficit, altered sensorium and with evidence of venous sinus thrombosis on Magnetic Resonance Venography (MRV) were included in the study. However, patients with cavernous sinus thrombosis, incomplete clinical or radiological record, inconclusive radiological findings were excluded from the study. Patients presenting within 48 hours were considered to have acute onset, while patients with onset longer than 48 hours but less than one month were considered sub acute, and patients with onset more than one month were considered chronic.

A complete history was taken from the enrolled patients and were studied for their demographic profile. A detailed examination including fundus examination was done and patients were subjected to various tests like complete blood count, blood sugar, renal function tests, liver function tests, prothrombin time, activated partial thromboplastin time, 12 lead electrocardiogram, X-ray chest, Computed Tomography head/Magnetic Resonance brain, MRV, CT angiography, and Protein C, Protein S, Antithrombin III, Homocysteine levels,

Factor V Leiden and Anticardiolipin antibodies wherever possible.

Protein C, Protein S and Antithrombin III were done after 6 months of acute event and after stopping oral anti-coagulants for 2 weeks. Patients were followed up for minimum period of 6 months and outcome was assessed on basis of morbidity and mortality on follow-up. Morbidity was assessed by using Rankin disability score (RDS) at time of discharge and follow-up<sup>(16)</sup>. Patients were categorized as having no disability, mild disability, moderate disability and severe disability on basis of RDS.

### Results

The general characters of subjects, clinical symptoms and etiological factors are summarized in Table 1. Out of 36 patients in study group, 24 (66%) patients were in the age group 19-40 years. The mean age of the patients was 35.5 years with range of 19-68 years. 32 (88.8%) patients were females and 4 (11.2%) were males. Out of 32 female patients in the study, 12 (33.33%) female patients had puerperium as a risk factor while as oral contraceptive use as an etiological factor was present in 6(16.6%) female subjects. Antiphospholipid antibodies (APLA) were found in 4 (11.11%) female patients particularly who had bad obstetric history. 2 patients were found to have polycythaemia as a predisposing factor and 2 had metastatic disease. 2 patients had tested positive for methylene tetrahydrofolate reductase (MTHFR) gene mutation while another 2 patient had deficiency of protein C, protein S and Antithrombin III. Assessment of symptoms showed that the most common symptom was headache which was present in 34 patients comprising 94.44% of total patients. Convulsions were present in 30 patients constituting 83.33% of total subjects in the study group and hemiparesis was present in 22 (61.11%) and tripareisis in 2 (0.05%) patients. Papilledema and altered sensorium was found in 20 patients (55.55%).

In this study, at the time of discharge 18 patients (50% patients) had RDS of 0 and 1 and thus no

disability. 2 patients had RDS of 2 hence falling into mild disability group and 2 patients had RDS of 3-4, hence falling into moderate disability group. None of the patients had a severe disability at the time of discharge (RDS >4). At the time of discharge 30 patients were alive (83.33%) and six patients died (16.66%).

In present study, 12 patients presented within 48 hours of onset of symptoms comprising 33.33% of total population in the study group. 16 patients presented within 48 hours to 7 days of onset of symptoms constituting 48.7% of total population in study group and 4 patients presented within 7 to 14 days of onset of symptoms comprising 11.11% of total patients. 3 patient's presents within 14 to 30 days of symptom onset and 1 patient presented after 30 days of symptom onset.

Clinical and diagnostic parameters of patients are summarised in Table 2. Among the different clinical factors, 25 patients were anaemic and the percentage of mortality was higher when there was moderate to severe anaemia. The death rate 66.66% when Haemoglobin value was <10 gm%. 01 patient had died during six months of follow-up and 29 patients were alive at the end of six months. 09 patients had headache on followup. Focal neurological deficit persisted in 07 patients and convulsions occurred in 04 patients on follow up.

Altered sensorium at the time of admission was present in 43.5% of patients (20 subjects). 23 patients (50%) had papilledema and 12 patients (26.1%) had hemiparesis in the study group. 02 patients had monoparesis and 01 patient had quadripareisis at the time of admission. 04 patients (8.7%) had cranial nerve paralysis, out of which 03 had abducens nerve palsy and 01 had oculomotor nerve palsy. MRI of brain showed that out of 36 patients, 20 patients (55.55%) had hemorrhagic infarction while 08 patients had (22.22%) had non-hemorrhagic venous infarction. Another 08 patients (22.22%) had intracranial haemorrhage only. Mass effect was seen in 12 patients accounting for 33.33% of all patients and

bilateral infarct was seen in 06 patients comprising 16.66% of all patients.

A good number (66.66%) of individuals were involved in superior sagittal sinus in combination with sigmoid and straight sinus. The transverse sinus was involved in 08 patient (22.22%) and straight sinus and deep cerebral vein were thrombosed in 02 patients each (0.05%)(Table 2).

**Table 1:** General characteristics, symptoms and etiology of CVST in Kashmir-India (2014-2016)

Variable	Number (n=36)	(%age)
<b>Gender</b>		
Male	04	11.11
Female	32	88.88
<b>Age (years)</b>		
18-30	10	27.78
31-40	14	38.89
41-50	06	16.66
51-60	04	11.11
>60	02	0.05
<b>Signs and Symptoms</b>		
Headache	34	94.44
Seizures	30	83.33
Hemiparesis	22	61.11
Papilledema	20	55.55
Altered sensorium	20	55.55
Triparesis	02	0.05
<b>Duration of Disease</b>		
Less than 48 hours	12	33.33
48 hours to 7 days	16	44.44
7 days to 14 days	04	11.11
14 days to 30 days	03	0.08
>30 days	01	0.02
<b>Etiology</b>		
Idiopathic	04	16.16
Puerperium	12	33.33
Oral contraceptive	06	16.66
Antiphospholipid antibodies	04	11.11
MTHFR mutation	02	0.05
Polycythaemia	02	0.05
Disseminated Malignancy	02	0.05
Protein C and S deficiency	02	0.05
Infections	02	5.5
<b>Level of consciousness</b>		
Fully conscious	04	11.11
Drowsy	18	
Unconscious with purposive movements	10	27.78
Deeply comatose	04	11.11

**Table 2:** Clinical and diagnostic characteristics of subjects with CVST (2014-2016)

Variable	No. of patients	%age
<b>Haemoglobin gm%</b>		
≤5	00	0.0
5 -8	06	16.66
8.1-10	14	38.89
>10	16	44.44
<b>CSF changes</b>		
Normal	05	13.89
Polymorphic pleocytosis	02	0.05
Lymphocyticpleocytosis	01	2.78
Haemorrhagic CSF	00	0.0
<b>Rankin Disability Score</b>		
0 & 1 (no disability)	18	50.0
2 (mild disability)	02	0.05
3-4 (moderate disability)	02	0.05
>4 (severe disability)	00	0.0
<b>MRI Finding</b>		
Haemorrhagic Infract	20	55.55
Infract	08	22.22
Haemorrhage	08	22.22
Unilateral lesions	26	72.22
Bilateral lesions	10	27.78
<b>Location of thrombus</b>		
Superior sagittal+sigmoid+straight sinus	24	66.66
Sigmoid sinus	8	22.22
Straight sinus	2	0.05
Deep cerebral vein	2	0.05

**Discussion**

In this study 36 subjects with CVST were studied, purpuriem remains the leading risk factor and 18-40 years age group is the most affected group. Most of the patients presented with more than one symptom and with variable duration but headache being the most common symptom. Headache appeared to be common in CVST. In the present study headache was seen in 94% of patients which was in agreement with previous studies (2,17). Clinical presentation of CVST is extremely variable, ranging from isolated headache to focal deficits to encephalopathy to psychiatric manifestations to coma (2,8,18-20). Clinical presentation of our cohort is almost identical to what has been reported from the west. 88.88% percent of our patients had mental status changes including drowsiness, confusion, and agitation, as compared to 22% reported in International Study on Cerebral Venous and Dural Sinus Thrombosis

(ISCVT)<sup>(21,22)</sup>. We noted a median duration from symptom onset to hospital presentation as 5 days, as compared to 4 days in other reports<sup>(21,22)</sup>. Douglas et al reported that frequency of peripartum intracranial venous thrombosis is 8.9 to 11.6 cases per 100 000 deliveries<sup>(23,24)</sup>. In our cohort 33.33% of the females were in the postpartum state as opposed to 15% reported from the west<sup>(21,25)</sup>. The plausible reason for this difference include home deliveries in unhygienic environments and certain rites like water deprivation during immediate postpartum period. In addition, because birth rates in our countries are higher than in the west, we might see more postpartum women. OCPs have long been attributed to development of CVST<sup>(4)</sup>. In our study only 16.66% of women were using oral contraceptives. This may simply reflect lack of use of oral contraceptives in our region of the world because of certain reasons including religious obligations. Thrombophilia is an important cause of CVST and has been reported in 15% to 22% of patients<sup>(22, 25)</sup>. In compliance to these studies we noted almost similar observations (22.22%) regarding genetic thrombophilia, however, the results were comparatively lower (12.5%) than noted by Daif et al from Saudi CVST subjects<sup>(26)</sup>.

In the current study 88.88% of CVST patients received anticoagulation. They were treated with intravenous heparin for 2 weeks followed by oral anticoagulation and duration of oral anticoagulation was decided on the basis of underlying etiology. In 4 patients we did not prefer intravenous heparin because of large and bilateral venous haemorrhagic infarcts. This is in accordance with that reported in ISCVT, which reported 85% as having received anticoagulation. In our study mortality was 16.66% i.e 6 out of 36 patients died which is almost equal to other western studies<sup>(22)</sup>. The predictors of unfavourable outcome were haemorrhagic infarctions and focal motor deficits and comatose states. There was also a trend that coma at presentation and involvement of deep cerebral venous system was associated

with poor outcome. Similar trends have been reported in the literature<sup>(9, 22)</sup>. We noted a death rate of 16% at discharge, which is within the range reported in earlier studies, i.e, 4.3% to 15%<sup>(21)</sup>. We found coma to be an independent predictor of death at discharge, and there was also trend that patient's older than 45 years were more likely to die during the hospital stay.

Follow-up was available for all 30 patients of our study. 85% had no disability on follow-up. Proportion of complete or near complete recovery is similar to that reported earlier<sup>(27,28)</sup>.

Mehta SR et al, reported the almost similar number of deaths as found in the current study<sup>(29)</sup>. In our study, at presentation 04 patients were fully conscious, two were having headache with papilloedema, 01 presented with seizure and another with headache only. Four patients were brought in deeply comatose state, out of them 3 patients died.

### Conclusion

CVST is an important cause of stroke in young especially in the peripartum settings, yet it is grossly under recognized. It may occur in absence of demonstrable cause, may occur in settings of hematologic disorder/coagulation abnormality, OCP use or may result from local contiguous infections process. Apart from its diverse causes, its varied presentations necessitate one to have a strong degree of suspicion in appropriate context. Once the diagnosis is made, it has a good prognosis but early treatment like anti edema measures and judicious use of heparin needs to be taken care off.

Small sample size is the main limitation of our study. However, to our best knowledge such type of study is being executed first time in Kashmiri subjects.

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