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## RESEARCH ARTICLE

### THE CLINICAL PROFILE IN MALE CVT PATIENTS ADMITTED TO THE INSTITUTE OF NEUROLOGY, MADRAS MEDICAL COLLEGE, INDIA

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## INTRODUCTION

Cerebral venous thrombosis (CVT) is an uncommon cause of stroke and an important cause of stroke in young. The Exact etiology and prevalence of the disease are yet to be fully understood. However various risk factors that predispose to the development of CVT have been identified. The first description of CVT was provided by Ribes in a 45-year-old man who had a constellation of severe headache, delirium and

epilepsy in the year 1825 (Ribes, 1825). Based on studies available it is estimated that CVT occurs in 5 people per million and contributes to 0.5% all strokes (Boussier, 2007). Studies have shown that the prevalence is higher in Asia compared to the western population. The Studies from India show that CVT is seen in 4.5/1000 deliveries and contributes to 10% of all stroke (Banerjee, 1989; Bansal 1980).

#### ABSTRACT

**Background:** Cerebral venous thrombosis (CVT) is an important cause of stroke in young. The Exact etiology and prevalence of the disease are yet to be fully understood. However various risk factors that predispose to the development of CVT have been identified. Cerebral venous thrombosis is most commonly seen in females, now there is no gender disparity. **Objective:** To study the clinical profile in male CVT patients admitted to the Institute of Neurology, Madras Medical College, India Materials and method: Clinical characteristics of 203 consecutive male patients diagnosed to have CVT and proven by MRI were analyzed who were admitted in the Institute of Neurology, Madras medical college, India. Data obtained a s an Asian CVT registry questionnaire. Clinical profile and risk factors are studied. **Results:** The mean age of male patients with CVT was (38 + 6.9 years). Out of 203 patients, 147 patients (72.4%) were aged less than 40 years. The most common clinical feature encountered is Headache (93.5%). Papilledema was observed in 101 patients (50.2%). Trans-Venous Aphasia was observed in 21 patients (10.3%). Cranial nerve abnormality was observed in 70 patients (34.7%). Seizures developed in 101 patients (49. 7%) and the majority of them had 2 or fewer episodes (59%). The generalized tonic-clonic seizure was the most common semiology observed (82 patients). Focal seizures were observed in 17 patients and 2 had status epilepticus .61 patients (30%) had motor weakness on examination. Ataxia and vertigo noted in 8 patients (3.9%). All patients had evidence of venous sinus thrombosis in MR venography. The most common venous system is the superficial venous system (98.7%). The most common vein affected is superior sagittal sinus (68.3%) followed by Transverse sagittal sinus (53.6%). Iatrogenic antithrombotic therapy-related hemorrhage was seen in 6 patients (4 GI bleed and 2 Hematuria) and was not severe warranting transfusion. The nosocomial infection developed in 4 patients (2 UTI and 2 Aspiration Pneumonia).Malignancy is noted in one patient.4 patient expired in spite of therapy (2 due to aspiration pneumonia, 1 due to a rapid worsening of neurological status and 1 due to the development of pulmonary embolism). **Conclusion:** Compare to previous International study, Incidence of CVT in Male's are higher. Alcoholism is a major risk factor. Compared with previous Indian studies there is no significant difference in gender disparity, clinical profile and risk factors.

CVT, even though observed in both sexes, are more common in women due to gender-specific risk factors (GSRF) like puerperium, oral contraceptive consumption (OCP) and hormone replacement therapy (HRT). Even the earlier studies from India showed an increased incidence of CVT in women (Dash, 2015). However recent studies have shown an equal or higher incidence of CVT in men (Pai, 2013; Narayan *et al.*, 2012). Thrombophilic state (genetic or acquired) is observed as the most common etiological factor for CVT in men (Boussier, 2007; Ferro *et al.*, 2004; Narayan *et al.*, 2012; Lim *et al.*, 2016; SK, 2017; Martinelli, 2003; Ventura, 2004).

**Aim:** To study the clinical profile in male CVT patients admitted to the Institute of Neurology, Madras Medical College, India

## METHODS AND METHODOLOGY

Clinical characteristics of 203 consecutive male patients diagnosed to have CVT and proven by MRI were analyzed who were admitted in the Institute of Neurology, Madras medical college, India. The method of our study is a prospective observational study. We collected data from the year 2015 to 2018. Data obtained as an Asian CVT registry questionnaire. Descriptive statistical analysis was performed using SPSS software version 19.0. Madras Institute of Neurology collects CVT data as a part of the Asian CVT registry (12-page questionnaire). 293 cases registered so far (203 men and 90 women). Intracranial hemorrhage, mental status abnormalities, GCS < 9, associated malignancy, deep venous system thrombosis, co-existing CNS infection are the following clinical symptoms and signs are considered as poor prognostic factors in Male CVT. Complete details regarding the patient were taken. All the patients are subjected to both CT brain and MRI brain with an MRI venogram.

## RESULTS

The mean age of male patients with CVT was (38 + 6.9 years). Out of 203 patients, 147 patients (72.4%) were aged less than 40 years. The most common clinical feature encountered is Headache (93.5%). A majority had headaches lasting for less than a week (42.6%). The most common type of headache was diffuse (30.2%) followed by a thunderclap and localized (25% & 24% respectively). Papilledema was observed in 101 patients (50.2%). Trans-Venous Aphasia was observed in 21 patients (10.3%). Wernicke's Aphasia is seen in 8 patients (38%). Cranial nerve abnormality was observed in 70 patients (34.7%).

The most common cranial nerve deficit is the combination of third, fourth and sixth cranial nerve palsy (18.2%). Seventh cranial palsy is seen in 13.3%. Lower cranial nerve palsy includes ninth and tenth cranial nerve is seen in 4.4%. Seizures developed in 101 patients (49.7%) and a majority of them had 2 or fewer episodes (59%). The generalized tonic-clonic seizure was the most common semiology observed (82 patients). Focal seizures were observed in 17 patients and 2 had status epilepticus. 61 patients (30%) had motor weakness on examination. Ataxia and vertigo noted in 8 patients (3.9%). All patients had evidence of venous sinus thrombosis in MR venography. The most common venous system is the Superficial venous system (98.7%). 8.3% of the patients had normal parenchyma. The most common vein affected is

superior sagittal sinus (68.3%) followed by Transverse sagittal sinus (53.6%).

**Table 1. Distribution of co-morbidities and risk factors in patients with CVT**

	Number (%)
Alcohol consumption	112 (55.2%)
Cigarette smoking	78 (38.4%)
Other substance abuse (Hans, gutka)	27 (13.3%)
Hypertension	24 (11.8%)
Head trauma	17 (8.4%)
Hematological disorders	11 (5.4%)
Diabetes Mellitus	10 (4.9%)
Tobacco chewing	6 (3%)
Coronary artery disease	4 (2%)
DVT	2 (1%)

**Table 2. Clinical features and neurodeficits in patients with CVT (N=203)**

Clinical feature	Number (%)
Headache	190 (93.5%)
Vomiting	94 (46.3%)
Visual complaints	54 (26.6%)
Altered sensorium	34 (16.7%)
Cranial Nerve deficits	
III, IV, VI palsy	37 (18.2%)
VI (isolated) palsy	19 (9.4%)
VII palsy	27 (13.3%)
IX, X palsy	9 (4.4%)
Nausea (Isolated)	25 (12.3%)
Aphasia	21 (10.3%)
Wernicke's aphasia	8
Broca's aphasia	6
Global aphasia	3
Mixed aphasia	2
Transcortical motor aphasia	1
Anomic aphasia	1
Fever	18 (8.9%)
Photophobia	13 (6.4%)
Phonophobia	8 (3.9%)
Behavioral changes	8 (3.9%)
Ataxia & Vertigo	8 (3.9%)

**Table 3. MRI findings in patients with CVT (N=203)**

MRI changes	Number (%)
Venous system involved	
Superficial venous system	99 (98.7%)
Deep venous system	44 (21.5%)
Mixed involvement	60 (29.6%)
Infarct/	76 (37.4%)
Infarct with hemorrhagic transformation	
Parenchymal hemorrhage (isolated)	38 (19.6%)
Normal parenchyma	17 (8.3%)
Vein affected	
Superior Sagittal Sinus	139 (68.3%)
Transverse Sagittal Sinus	109 (53.6%)
Sigmoid Sinus	54 (26.8%)
Cortical Vein	8 (3.9%)
Straight Sinus	16 (7.9%)
Internal Jugular Vein	12 (6%)
Cavernous Sinus	4 (1.9%)
Midline shift	7 (3.4%)
Hydrocephalus	2 (1%)
Others(4 had orbital cellulitis, 1 had transtentorial herniation)	5 (2.5%)

Iatrogenic antithrombotic therapy-related hemorrhage was seen in 6 patients (4 GI bleed and 2 Hematuria) and was not severe warranting transfusion. The nosocomial infection developed in 4 patients (2 UTI and 2 Aspiration Pneumonia). Malignancy is noted in one patient. 4 patient expired in spite of therapy (2 due to aspiration pneumonia, 1 due to a rapid worsening of

neurological status and 1 due to development of pulmonary embolism) (Table 1 to 4).

**Table 4. Distribution of poor prognostic factors and adverse clinical outcomes in patients with CVT (N=203)**

	Number (%)
<i>Poor prognostic factors (clinical variables)</i>	
Deep venous system involvement	104 (51.3%)
Intra cranial hemorrhage	86 (42.3%)
Mental status disorder	15 (7.5%)
GCS < 6	12 (6%)
CNS infection	2 (1%)
Malignancy	1 (0.5%)
<i>Adverse clinical outcomes</i>	
Rapid progression to coma	7 (3.4%)
Anti thrombotic therapy related hemorrhage	6 (3%)
Worsening hemorrhage (in spite of treatment)	4 (2%)
Nosocomial infection	4 (2%)
Requirement for Mechanical Ventilation	3 (1.5%)
Development of DVT or Pulmonary Embolism	1 (0.5%)
Death	4 (2%)

## DISCUSSION

The cerebral venous thrombosis is most often common in young adults and children. Females are more affected than males. The annual incidence is 3 - 4 per 1 million population and 7 per 1 million among children (Thrombosis, 2005). The most common age group was 20-50 years and less than 10% are older age group. 85% of the cerebral venous thrombosis is due to prothrombotic conditions. The cerebral venous thrombosis risk is increased in the last trimester and immediately after delivery in females. Third generation OCP intake has a higher risk for CVT. Dehydration, infections, Pregnancy, puerperium, malignancy, AV malformations, trauma, neurosurgical interventions are the other risk factors associated with CVT. Alcoholism, hyperhomocysteinemia, and drug abuse were the most common risk factors encountered in males. The occlusion of cerebral veins results in edema and venous infarction. The occlusion of major sinuses results in an increase in intracranial tension. Alcohol results in dehydration, reactive thrombocytosis, and hypercoagulability which in turn cause cerebral venous thrombosis (Thrombosis of the cerebral veins and sinuses, 2005). Headache is the most common presenting symptom of CVT. CT venography or MRI brain and MR Venogram is the investigation of choice.

The Dense triangle sign, cord sign, empty delta sign are the various signs noted in the CT brain. Hyperintense signals are noted in T2 weighted images in the MRI brain. The absence of flow voids is noted in the MR venogram. Intravenous heparin is the treatment of choice. Oral anticoagulants are given at least for 6 months and to maintain an International normalized ratio to 2.5. Antiepileptic drugs are used to treat the patients presented with seizures. Surgical options like Endovascular thrombolysis with the thrombolytic enzyme, Urokinase can be tried. Poor prognosis is associated with intracerebral hemorrhage and impairment of consciousness (Thrombosis of the cerebral veins and sinuses, 2005). A study by Pai *et al.*, (2013) is an Indian study conducted in Mumbai from 2001 to 2010 and included 612 patients from various hospitals in Mumbai. One of the largest studies in India. Among 612 patients 354 were men, 219 were women, 39 were children.

Papilledema and headaches are the most common clinical manifestations noted. Superior sagittal sinus thrombosis followed by cortical venous thrombosis noted. Another study from India by Narayan *et al.* (2012) conducted in Nizam's Institute of Medical Sciences, Hyderabad between June 2002-September 2010. They included 428 patients, 230 were males and they concluded seizures is the most common presentation followed by stroke-like presentations. Anemia and alcoholism are the common risk factors encountered. Among prothrombotic conditions, hyperhomocysteinemia followed by Protein S deficiency noted. A prospective observational study conducted by Ferro *et al.* (2004) included 21 countries and 89 centers worldwide and they included 624 patients, 465 were females, Headache is the most common clinical presentation followed by seizures. Superior sagittal sinus thrombosis is the most commonly involved followed by transverse sinus thrombosis. Prothrombotic states are the most common risk factor observed and they also observed lumbar puncture, jugular catheter occlusion, and surgical procedure were also noted as risk factors. Comparing our study with western study, incidence among men is higher, however, Indian studies suggest incidence among Males are higher. The mean age of male patients with CVT in our study was (38 + 6.9 years) when compared with previous Indian study was 31.3 years. Headache is the most common clinical symptoms in our study, western data, and Mumbai based data. However Narayan *et al.*, seizures are the common presentation. Papilledema is the commonest clinical sign associated with cerebral venous thrombosis in all three studies. Ninth and Tenth Cranial nerve involvement is noted in our study. Paraparesis and quadriparesis are noted in Nizam's venous stroke registry; however, these symptoms are not seen in our study. In western data, Aphasia is noted in 19.1% including both males and females. In our study, 10.3% had aphasia in the male population (Transvenous aphasia, 2009). In other Indian data's Aphasia due to Cerebral venous thrombosis is not reported. Transverse sinus thrombosis is the most common vein involved as per western data. However, superior sagittal thrombosis is most commonly involved in our study. Patients with superficial venous system involvement with GCS>12 had a good prognosis when compared to low GCS and deep venous system involvement.

## Conclusion

Cerebral venous thrombosis is an important and treatable cause of stroke. Prognosis is generally favorable when compared with arterial stroke. Alcoholism is strongly associated with Male cerebral venous stroke. Aphasia is not reported in previous Indian studies. The registry is being updated on a daily basis to collect as much as data possible.

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