A study of clinical profile, etiology, therapeutic outcomes of patients with cerebral sinus venous thrombosis in men

E.A. Ashok Kumar1*, Manisha A2, Muppala Hanvitha3

1Professor, 2,3Post Graduate Student
Department of General Medicine, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana, India
*Corresponding author email: ashokedla@gmail.com

Abstract
Cerebral sinus venous thrombosis (CSVT) is very rare in men compared to women. There are many causes but they are very rare in men, and it is an uncommon cause of cerebral infarction. Patients usually present with Headache, Focal deficits such as Monoparesis, Hemiparesis, Paraparesis and Hemisensory disturbances, seizures, impairment of level of consciousness. Now it is recognized as a non-septic disorder with various clinical presentations with a favorable outcome, and low mortality rate below. CT scan, MRI and Magnetic Resonance Venography (MRV) are the best diagnostic methods for diagnosis and low molecular weight heparin is the first-line treatment. Results of this study, clinical profile, etiology, therapeutic outcomes of patients with cerebral sinus venous thrombosis in men are discussed.

Key words
Cerebral sinus venous thrombosis (CSVT), Men, CT scan, MRI and Magnetic Resonance Venography (MRV), Low molecular weight heparin.

Introduction
Cerebral sinus venous thrombosis (CSVT) is thrombosis of the venous channels in the brain; it is an uncommon cause of cerebral infarction. But it is an important consideration because of its potential morbidity [1]. It should be considered as a differential diagnosis of all unexplained CNS disorders of sudden onset [2].
Virchow’s triad which includes endothelial damage, stasis and hypercoagulability of blood may in turn have several contributory factors to produce the final manifestation as CSVT [2]. There are many causes for CSVT. Patients usually present with Headache, Focal deficits such as Monoparesis, Hemiparesis, Paraparesis and Hemisensory disturbances, seizures, impairment of level of consciousness [3, 4].

In the beginning of the 19th century, CSVT was thought to arise from infection which affected the superior sagittal sinus most commonly and resulted in bilateral or alternating focal deficits, seizures, and coma, finally led to death [5]. But now it is typically recognized as a non-septic disorder with various clinical presentations with a favorable outcome, and mortality rate below 10%. MRI and Magnetic Resonance Venography are the best diagnostic methods for diagnosis and low molecular weight heparin is the first-line treatment [6, 7]. Anticoagulation remains the principal therapy in preventing thrombus propagation and in increasing recanalization [8].

With the advent of CT scan brain and MRI and MR venography, many cases of CSVT are diagnosed early. Therefore it is important to be aware of different clinical presentations and course of CSVT, as most of them have good prognosis if they are treated early [5].

Despite of widespread availability of imaging, the diagnosis of CSVT is still overlooked because of the diversity of its clinical presentations, modes of onset, and neuroimaging signs, and cause is not found in about 15% of cases, hence it remains a diagnostic and therapeutic challenge [5].

In recent years, progress has been made in understanding CSVT from the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) - a multicentre prospective cohort of 624 adult patients which is the largest cohort study till today in CSVT [9]. This study of clinical profile, etiology, therapeutic outcomes of patients with cerebral sinus venous thrombosis in men is carried out to know the causes.

It is very rare in men compared to women and will help in diagnosing the cause, reducing the morbidity and mortality by emphasizing the need for compliance to medication and regular follow up and patient education [10]. There are many causes but they are very rare in men.

Aim and objectives
- To study etiology, clinical profile and imaging features in cerebral venous sinus thrombosis in men.
- To study treatment outcomes in patients with cerebral sinus venous thrombosis in men.

Materials and methods

Methodology
- Study design: Prospective Observational study.
- Study area: Department of General Medicine in Malla Reddy Institute of Medical Sciences, Hyderabad
- Study period: January 2021 to June 2022 (18 months)
- Sample size: 42 Cases

Inclusion criteria
- All male patients between 18 to 60 years showing signs, symptoms, imaging features consistent with cerebral sinus venous thrombosis.
- Patients who were willing to give consent.

Exclusion criteria
- All females.
- All males below the age of 18 years and above 60 years.
- All the patients with arterial or venous cerebral hemorrhages or arterial cerebral infarcts.
- Those who were not willing to give the consent.
Results

The present study was an observational study done in patients of CSVT in males who were admitted in Department of General Medicine at Malla Reddy Institute of Medical Sciences, Hyderabad. Study was done for a period of 18 months, in 42 patients. In this study 9% of them were in between 18-30 years, 16% were in between 31-40 years, 7% were in between 41-50 years, 10% were in between 51-60 years and most of them presented in the age group of 31-40 years. Most of the patients presented in summer months, 6% in January, 3% in February, 8% in March, 5% in April, 13% in May, 4% in June, 1% in August, November, December. During summer months it was in the month of May, the number of cases was the highest (Table – 1).

Table – 1: Distribution of cases in relation to month.

<table>
<thead>
<tr>
<th>Month</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>November</td>
<td>01</td>
</tr>
<tr>
<td>December</td>
<td>01</td>
</tr>
<tr>
<td>January</td>
<td>06</td>
</tr>
<tr>
<td>February</td>
<td>03</td>
</tr>
<tr>
<td>March</td>
<td>08</td>
</tr>
<tr>
<td>April</td>
<td>05</td>
</tr>
<tr>
<td>May</td>
<td>13</td>
</tr>
<tr>
<td>June</td>
<td>04</td>
</tr>
<tr>
<td>August</td>
<td>01</td>
</tr>
</tbody>
</table>

Table – 2: Distribution of cases in relation to symptom.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>25</td>
</tr>
<tr>
<td>Seizures</td>
<td>15</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>01</td>
</tr>
<tr>
<td>Acute gastro enteritis with dehydration (moderate to severe)</td>
<td>15</td>
</tr>
</tbody>
</table>

In this study, 37% of them presented with transverse sinus thrombosis, 10% with sigmoid sinus and another 10% SSS and transverse sinus thrombosis was the most common sinus involved (Table – 3).

Table – 3: Number of sinuses involved.

<table>
<thead>
<tr>
<th>Sinuses involved</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse sinus</td>
<td>37</td>
</tr>
<tr>
<td>Sigmoid sinus</td>
<td>10</td>
</tr>
<tr>
<td>Superior sagittal sinus</td>
<td>10</td>
</tr>
</tbody>
</table>

It was noticed the correlation between hyponatremia and CSVT, of which 60% of them who had hyponatremia presented with CSVT, and in 40% had CSVT without hyponatremia due to dehydration (Table - 4).

Table – 4: Distribution of cases in relation to sodium.

<table>
<thead>
<tr>
<th>Hyponatremia</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>25</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
</tr>
</tbody>
</table>

In this study, there were no autoimmune etiologies, The Anti-cardiolipin Antibodies were negative, Anti-phospholipid Antibodies were negative, Anti-ds DNA n were negative, Anti-Thrombin III were negative and Protein ‘C’ and Protein ‘S’ were also negative.

The main risk factor was dehydration due to acute gastroenteritis, vomiting. Interestingly we found one case of CNS tuberculoma with CSVT.

Discussion

The present study was an observational study done in patients of CSVT in males who were admitted in Department of General Medicine at Malla Reddy Institute of Medical Sciences, Hyderabad. The study was done for a period of 18 months, in 42 patients. In this study 9% of patients were in between 18-30 years of age, 16% were in between 31-40 years, 7% were in between 41-50 years, 10 % were in between 51-60 years and more number in the age was found...
in the age group of 31-40 years, which is similar to Girot, et al. study in ISCVT trial showed around 40 years of age [11]. However, the mean age was lower in Narayan, et al. study [5] conducted at Nizams Institute of Medical Sciences which is about 31.3 years.

CSVT in males, which was in consonance with Narayan, et al. study [5] and similar results were seen in Parikh, et al. [12], Navin Pai, et al., in his study showed similar trend i.e.; in 612 consecutive patients of CSVT from various hospitals of Mumbai had a male to female ratio of 3:2 [13] all of which had male dominance. CSVT is more common in females because of Pregnancy, Estrogen, Hypothyroidism, and APLA syndromes but men will not have all these causes like Pregnancy, Estrogen, Hypothyroidism. APLA syndromes in western countries associated with puerperium according to Guenther, et al. [14] study. The studies done by Wassay, et al. [15] and Ferro, et al. [9] in ISCVT trial showed larger proportion of females. Even earlier studies from India had female predominance. According to Narayan, et al.; the study done in India which included 428 patients there was a declining trend of CSVT in postpartum state due to increased obstetric care [5].

In this study, most of the men presented in summer months, 6% in January, 3% in February, 8% in March, 5% in April, 13% in May, 4% in June, 1% in August, November, December. Among summer months, it was in the month of May, the number of cases were maximum. CSVT is most common in males during summer months because of dehydration and their outdoor working during summer months. There are many causes of dehydration during summer months, like lack of potable drinking water, water supply is not continuous. There is increase in cases of diarrhea and gastroenteritis because of contamination of water and when the water resources become scarce. Dehydration secondary to severe gastroenteritis is a risk factor for CSVT in adults. Early diagnosis of CSVT relies on a high index of suspicion, the recognition of risk factors, and a careful search for signs of CSVT on CT images [16]. In our study, dehydration secondary to acute GE was found in 15% of cases.

A study showed that heat stroke can cause CSVT with cerebral magnetic resonance venography (MRV) showed the development of CSVT. Therefore, cerebral MRI findings in heat stroke must be assessed; in addition, early MRV can help in the diagnosis of the disease, which can effectively improve prognosis. Severe heat stroke can be life-threatening, and nearly 30% of survivors present with permanent neurological sequelae [17].

As evidenced by Pai, et al. [13] and Narayan, et al. [5] studies, infective etiology of CSVT was the most common but due to introduction of broad spectrum antibiotics the overall incidence of infective CSVT has come down now in recent times. No etiology was found in about 13% of the patients [9], hence, the search for etiology in CSVT remains a difficult problem.

In this study, there were no cases of autoimmune etiology, The Anti-cardiolipin antibodies, Anti-phospholipid Antibodies, Anti-ds DNA, Antithrombin III, Protein C and Protein S were negative in all the cases studied.

Throughout the world the most common risk factor identified for CSVT is prothrombotic condition. Narayan, et al. also reported that 12.3% patients had genetic prothrombotic condition as a risk factor for CSVT [5]. In the cohort study of ISCVT, a prothrombotic condition was found in 34% of all patients, and a genetic prothrombotic condition was found in 22% of all the patients [9]. No proper data is available about prothrombotic conditions in earlier studies conducted in India.

Pai, et al. [13] in a study done in recent times, in Mumbai over a period of 9 years, tested the cohort for common thrombophilia markers Protein ‘C’, Protein ‘S’, Anti-thrombin III, and Factor V Leiden (FVL) mutation. Among 18% of
the patients who were positive for the thrombophilia markers, Protein ‘C’ deficiency was the most common thrombophilia marker followed by a deficiency of Protein ‘S’, Factor V Leiden mutation, and Anti-thrombin III deficiency.

The various causes of CSVT are Dehydration, Infection, Trauma, Pregnancy and Puerperium, Inflammatory Bowel Diseases, hematological conditions like Paroxysmal Nocturnal Hemoglobinuria, Polycytemia, Sickle Cell Anemia, Collagen vascular diseases, Nephrotic syndrome, Cirrhosis of Liver and Hypercoagulable states like Anti-phospholipid antibody syndrome, Protein ‘C’ and protein ‘S’ deficiency, Anti-thrombin III deficiency, Factor V leiden mutation [2]. Neighbourhood syndromes because of Mastoiditis, Cerebral Abcess, Tuberculomas [18] and Hypervitaminosis D [19] also cause CSVT.

Headache was the presenting symptom in 70–90% of cases. Its pathophysiology lies in the venous walls distension or due to local inflammation or the blood leakage over the brain surface irritating dural sensitive fibers [20]. In this study also headache has been the most common presenting symptom. Next to headache seizures has been the second most common symptom, 25% presented with headache, 15% with seizures and 1 case with hemiplegia. Other symptoms include seizures, vomiting, nausea, focal neurological deficits like Monoparesis, Hemiparesis, Paraparesis and Hemisensory disturbances, developing mild confusion to progressive coma [1, 20]. The most frequent, the earliest symptom of CSVT is headache. In the NIVSR cohort study, 88.3% patients had headache as the presenting complaint with SVT [9]. According to Girot, et al. [11] study in ISCVT trail, seizures was noticed in 55% of patients. However, according to NIVSR cohort done by Narayan, et al. [5] which included all CSVT patients headache, vomiting, and seizures were the most common symptoms found in 378 (88.3%), 298 (69.6%), and 171 (39.9%) patients, respectively. Headache is presented as acute, sub-acute, chronic or may even have a thunderclap-like presentation. In most cases, headache precedes the development of all other features by days, weeks and sometimes even months.

In this study, it was noticed the correlation between hyponatremia and CSVT, of which 60% of them who had hyponatremia presented with CSVT. In this study, a rare case was seen with both CSVT and CNS tuberculoma in a patient who presented with headache and seizures as presenting symptoms and dehydration due to acute gastroenteritis were risk factors.

Normally, the CSF drains into the SSS through the arachnoid granulations. When the thrombosis happens, the venous pressure raises due to delaying in the venous emptying, altering the CSF absorption, and thereby raising the intracranial pressure which inturn causes intracranial hypertension (ICH) [14, 21]. Symptoms are determined by the collateral blood drainage. When collaterals are sufficient, symptoms are related to ICH; when they become insufficient, the venous congestion causes ischemia and infarctions [14].

In younger patients, the spectrum of CSVT can range from venous congestion detectable or not on neuroimaging, to the parenchymal cortical or subcortical ischemic injury, less frequently CSVT-related sub-arachnoid and subdural hemorrhages are observed [22].

The International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) determined the frequency of the sites of CSVT as follows: Transverse sinus 86%, superior sagittal sinus 62%, straight sinus 18%, cortical veins 17%, jugular veins 12%, vein of Galen and internal brain veins 11% [9]. In this study 37% of them presented with transverse sinus thrombosis, 10% with sigmoid sinus and another 10% SSS and transverse sinus thrombosis is the most common sinus involved. This transverse sinus is most commonly involved because of the horizontal
nature where stagnation and sluggishness of blood flow is present.

In Kumar, et al. study, SSS was involved in 50%, transverse in 54%, sigmoid in 42% both of above are international studies [23]. However, in Indian studies, Narayan, et al. which included all CSVT patients sinuses commonly involved in the order are SSS (54%), right transverse (31%), sigmoid sinus (20.6%), left transverse (16.7%) again this difference can be attributed to inclusion of all types of CSVT [5].

For initial screening CT brain is used in patients with an acute neurologic deficit [24].

For diagnosis of CSVT, calculated sensitivity and specificity of CT scan is 68% and 52%, respectively [17]. In Acute CSVT primary sign of a plain CT is hyperdensity of a cortical vein or dural sinus. Approximately one third of CSVT shows hyperdense dural sinus [25, 26, 27]. Dense triangle, the dense or delta sign appears as thrombosis of the posterior portion of the superior sagittal sinus [28].

MRI is more sensitive than CT at each stage for detection of thrombus in a venous sinus and it may include a “hyper intense vein sign. The most commonly used method for imaging cerebral veins is MRV as it has short time of acquisition, large covering volume, good spatial resolution. When slices are perpendicular to the direction of flow then optimal signal is obtained [21].

A Randomized trial in Netherlands compared low molecular weight heparin with placebo in the management of CSVT and it showed that Patients who were treated with anticoagulants (low-molecular-weight heparin followed by oral anticoagulation) had a favorable outcome than the controls [29]. In this study, we gave injection Clexane 0.6 cc for 5 days, with these patients symptomatically improved.

The occurrence of CSVT during summer season can be prevented by simple measures like salted butter milk.

**Conclusion**

CSVT is one of the most common causes of cerebral infarction and should be considered in differential diagnosis of all unexplained CNS disorder of sudden onset. Patients usually present with headache, seizures, monoparesis, hemiparesis and paraparesis. Typically it is recognized as a non-septic disorder with various clinical presentations with favorable outcome. With the advent of new technologies like CT scan and MR Venography are the best diagnostic methods and Low Molecular Weight Heparin is the first line of treatment. Despite the widespread availability of imaging, the diagnosis of CSVT is overlooked because of the diversity of its clinical presentations. CSVT is common in females that too in young primipara’s at peripartum period. In males it is uncommon, but in summer months because of dehydration, heat exhaustion, gastroenteritis and diarrhea which may cause hyponatremia, which in-turn causes CSVT. Anticoagulation reduces the risk of fatal outcome, without promoting intracerebral hemorrhage. CSVT also occurs post SARS-CoV-2 Vaccination.

**References**


