

Clinical and neuroimaging correlation in patients with cerebral sinus venous thrombosis

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Abstract: *Objectives:* To study the clinical and neuroimaging correlation in patients with cerebral sinus venous thrombosis. *Methods:* Clinically suspected 50 patients of CSVT, were subjected to neuro imaging techniques, fulfilling the study criteria were recruited by simple random sampling and data collected was analyzed by correlational studies. *Results:* Of the 50 patients, 29 (58%) were females and 21 (42%) were males, and the mean age was 29.7 years, with maximum incidence of 87.5% in age group 20-40 years. Most common symptoms were headache 88%, seizures 66%, focal deficits 54%, altered sensorium 52% and mode of presentation was sub acute in 46% cases. Radiologically most common sinus involved was superior sagittal sinus 70%. 5 patients died during hospitalization. Out of the survived patients 35 patients (70%) had complete recovery. Poor prognostic factors at the time of admission were stupor and coma and evidence of haemorrhagic infarction in primary CT scan. *Conclusion:* Clinical manifestations, prognostic factors, common involved sinuses and image findings of this study were similar to those of other studies. Overall prognosis was good, but small percentage of patients died. Management with heparin and oral anticoagulants is safe and effective.

Keywords: Cerebral venous thrombosis, Clinical manifestations, Radiological findings, acute stroke, anticoagulation.

Introduction

Cerebral sinus venous thrombosis (CSVT) is an uncommon condition. Its clinical presentation is varied and often dramatic. It often affects young to middle-aged patients, and more commonly women. Although recognized for more than 100 years, it has only in recent years come to be diagnosed frequently ante-mortem. This is partly due to greater awareness among physicians and neurologists, and partly to improved non invasive imaging techniques. Occlusions of veins that drain were first published in 1820s. Ribes from France described the first case of dural sinus thrombosis [1].

A 45 year old man developed seizures, headache and delirium who died 6 months later and on autopsy he showed superior sagittal and lateral sinus were thrombosed and the brain showed carcinomatous metastasis. The annual incidence is currently estimated to be 3-4 cases per 1 million people. 3 out of 4 people with CSVT are women. It accounts for 10-20 % of the etiology of young strokes in India [2]. More than 100 causes of cerebral venous sinus thrombosis have been

recorded in the literature. However, even with extensive investigation no cause is identified in 20-25% of the cases [3]. CSVT presents with a wide spectrum of symptoms and signs. Headache is the presenting symptom in 70-90% of cases [3-5]. Focal deficits such as hemiparesis and hemisensory disturbance, seizures, impairment of level of consciousness and papilloedema occur in one-third to three-quarters of cases [3, 5] CSVT most commonly involves superior sagittal sinus (72%) followed by lateral sinus (70%). In 30 to 40% of cases more than one sinus is involved [6].

The diagnosis of CSVT requires high index of suspicion because of its varied presentations. Neuro imaging is the corner stone in the diagnosis of cerebral venous sinus thrombosis. Imaging modalities of choice in CSVT and CT scan and MRI with MRvenogram. CT scan may be normal in 15-30% cases but MRI with MRV is almost 100% diagnostic [7].

Current therapeutic options for CSVT treatment include anti-thrombotic therapy with un-fractionated heparin, low-molecular-

weight heparins (LMWH), oral anticoagulants, intravenous thrombolysis, local thrombolysis by selective sinus catheterization and a combination of thrombolysis and anticoagulation in addition to symptomatic therapy [8]. CSVT has an acute case fatality of less than 5% and almost 80% of patients recover without sequelae [9]. It has been found that early diagnosis of cerebral venous thrombosis is essential because early treatment may prevent morbidity and may even be life saving.

Therefore, a prospective observational study has been undertaken to describe the clinical profile, diagnosis and prognosis of CSVT.

Material and Methods

Source of data: 50 patients admitted to Basaveswara teaching and General Hospital, attached to M.R. Medical College, Gulbarga, between November 2012 to September 2014 with a confirmed diagnosis of cerebral venous thrombosis were taken up for the study and followed until discharge from the hospital or death. Discharged patients were followed up for a period of 6 months.

Method of collection of data: Meticulous history, clinical examination, laboratory investigations were carried out in all cases of cerebral venous sinus thrombosis. Cerebral venous thrombosis was confirmed by CT scan (or) conventional MRI (or) MR venogram.

Laboratory investigations

1. Complete blood count with peripheral smear (Hb, TC, DC, Platelet counts)
2. ESR
3. RBS
4. Serum urea
5. Serum creatinine
6. FLP, serum electrolytes, HIV.
7. Urine routine
8. ECG in all leads
9. CSF analysis (wherever deemed necessary)
10. BT, CT, Prothrombin time with INR, activated partial thromboplastin time.
11. CT scan
12. MRI and MR venogram.
13. Fundus examination.

Inclusion criteria

1. Patients with suspected cerebral venous thrombosis by clinical features,
2. Any age group presenting with Cerebral venous thrombosis,
3. Puerperal and non puerperal group.

Diagnostic criteria: Patients presenting with history and examination suggestive of cerebral venous thrombosis and confirmed by imaging of brain (CT scan direct and indirect signs, MRI, MRV).

A) Direct signs

- a. Hyperdense sinus on plain CT
- b. Cord sign on plain CT
- c. Empty delta sign on contrast enhanced CT
- d. Dense triangle sign on plain CT.

B) Indirect signs

- a. Cerebral edema
- b. Cerebral infarction not confirming to as arterial territory
- c. Cerebral haemorrhage
- d. Small ventricles
- e. Bilateral signs
- f. Gyral enhancement
- g. Territorial enhancement,
- h. Erosion of middle ear structures and changes in mastoid region.

Exclusion criteria

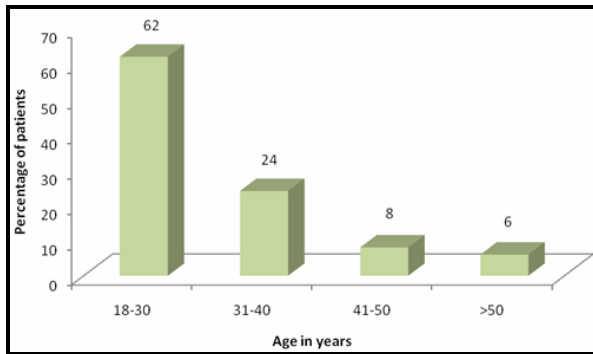
1. Hypertension,
2. Primary seizure disorder,
3. HIV positive patients,

The results were analysed by calculating percentages, the mean values, standard deviation, chi-square test. Proportions were compared using chi-square test and significance. A 'P' value of less than 0.05 was considered statistically significant.

Results

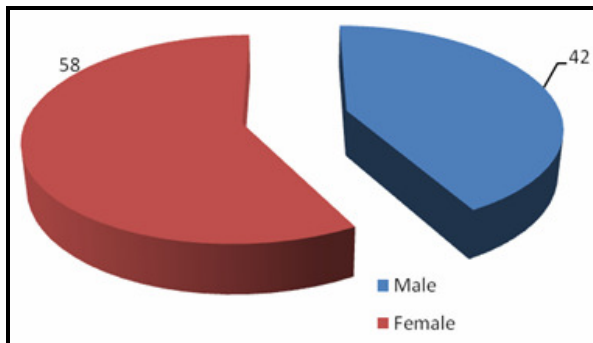
A total of 50 cases of cerebral sinus venous thrombosis were evaluated in the present study. The mean age of the patients in the present study was 29.7±8.4 Majority of them were in the age group of 18-30 contributing to 62.0%. The youngest being 18 and the eldest 59 years of age.

Figure-1: Bar graph showing Age Wise Distribution of Cases



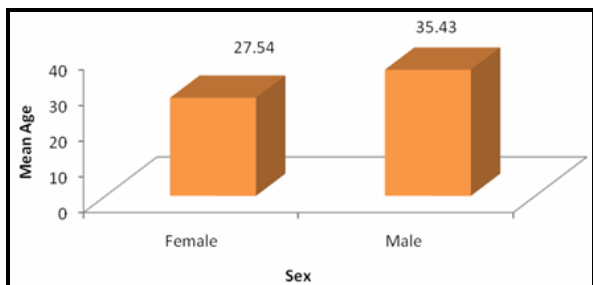
In the present study, Male: Female is 3:4.

Figure-2: Pie chart showing Sex Wise Distribution of Cases



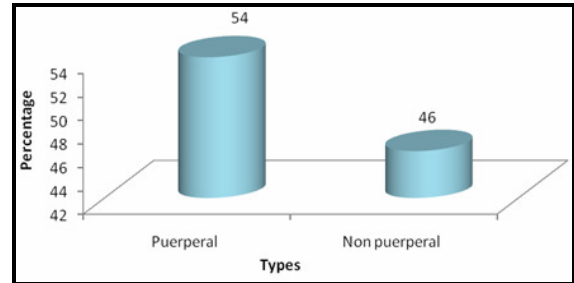
The mean age of female patients is 27.54 And male patients is 35.43 with a standard deviation of 5.7 and 10.3 respectively in the present study. $t=3.57$, $p<0.01$, highly significant difference of age among males and females.

Figure-3: Bar graph showing Mean Age of the Patients



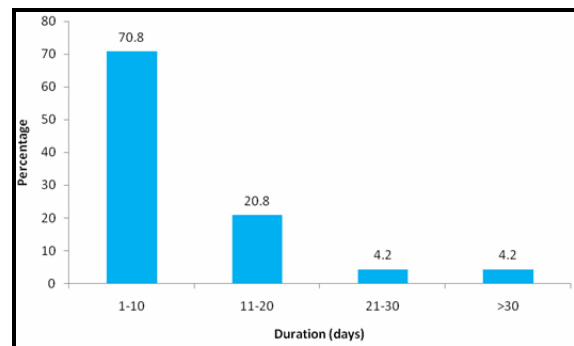
In the present study, out of 50, 27 (54.0%) patients belong to puerperal Group and 23 (46.0%) belong to non-puerperal group. Out of 23 non-puerperal, 4 were females, and 19 were male patients.

Figure-4: Bar graph showing Types of Csvt



In the present study, out of 24 puerperal patients, 70.8% (17 cases) of CVT occurred during 1-10 days after delivery. Followed by 20.8% (5 cases) of CVT occurred during 11-20 days.

Figure-5: Bar graph showing Duration from delivery on onset of symptoms



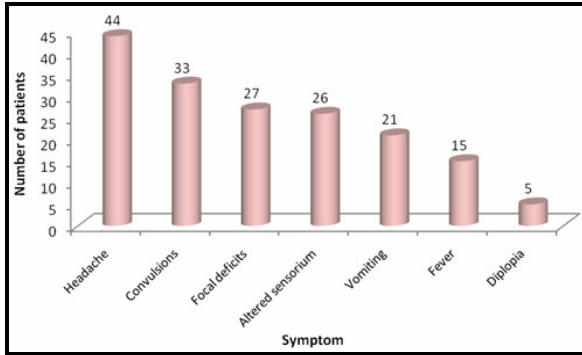
Those who presented within 48 hours were considered to have acute onset, with onset longer than 48 hours but less than 1 month were considered sub acute, and with onset more than month as chronic (Boussier [5] et al, 1985).

In the present study, 23 cases (46.0%) Of CSVT had subacute presentation, followed by 19 cases (38.0%) with acute presentation.

In the present study, 27 patients (54.0%) were conscious and 11 patients (22.0%) were drowsy, 7 patients (14.0%) Stuporous at the time of presentation.

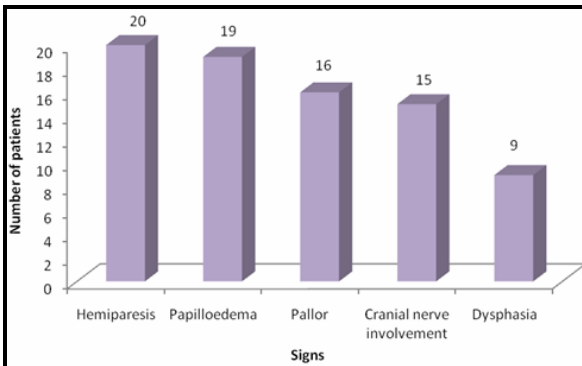
In the present study, most common symptom is headache present in 88% (44 cases) followed by convulsions in 66% (33 cases).

Figure-6: Bar graph showing Initial symptoms at presentation



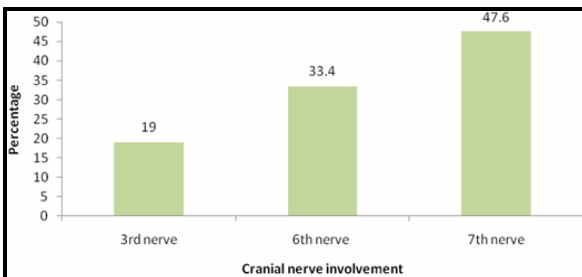
In the present study, hemi paresis was present in 40%, papilloedema in 38% and Dysphasia in 18.0% of patients.

Figure-7: Bar graph showing Clinical Signs at Presentation



Cranial nerve involvement	Number of patients	Percentage
3rd nerve	4	19.0
6 th nerve	7	33.4
7 th nerve	10	47.6
Total	21	100.0

Figure-8: Bar graph showing Cranial nerve involvement

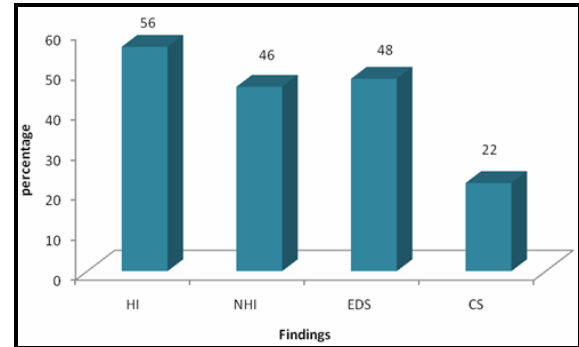


Hb% V/s patients mortality Chi-square 17.48, p<0.001 highly significant.

In the present study, out of 50 patients, 19 were anemic, accounting for 38.0% and the mortality was higher when the degree of anaemia was severe.

The investigative procedures like leucocyte count, blood sugar, serum creatinine, blood urea, liver function tests, serum electrolytes did not contribute to the diagnosis and were non-specific. In the present study, 28 cases (56.0%) had hemorrhagic infarction, followed by non-hemorrhagic infarction comprising 23 cases (46.0%).

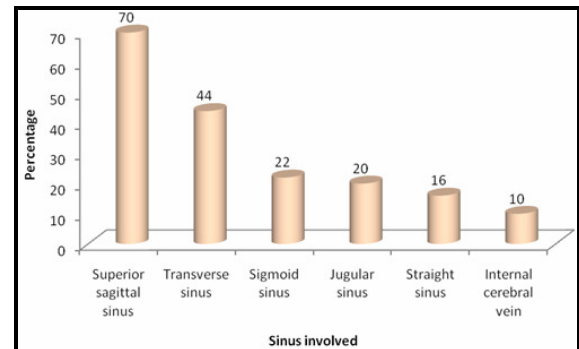
Figure-9: Bar graph showing CT and MRI findings



Nineteen patients were subjected to CSF analysis wherever there was suspicion of meningitis, out of which 12 (63.16%) were normal and pleocytosis seen in 4 (21.05%) patient and protein rise in 3 (15.78%) patients.

In the present study, the most common sinus involved was superior sagittal sinus in 35 Patients accounting to 70% followed by transverse sinus (44.0%) in 22 patients.

Figure-10: Sinus involvement (MRV)



Treatment: All the 50 patients were given anticoagulation, initially with subcutaneous LMWH in 33 cases (66%) and intravenous unfractionated heparin infusion in 18 cases (36%), later on changed over to oral anticoagulants. 5 patients (10%) required decompressive craniotomy, out of which one patient died. Additional treatments included anti epileptics in 35 patients (70%) and anti edema measures in 38 patients (76%). Mean hospital stay was 12.7 days in the present study.

Prognosis

Modified Rankin Scale (mRS): mRS is a commonly used scale for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability, and it has become the most widely used clinical outcome measure for stroke clinical trials. The scale runs from 0-6, running from perfect health without symptoms to death.

- 0 - No symptoms.
- 1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.

- 3 - Moderate disability. Requires some help, but able to walk unassisted.
- 4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
- 6 - Dead.

Mean hospital stay was 12.7 days in the present study (range 5-36). Modified Rankin scale score at discharge was : 16 have mRS score zero, 14 patients have mRS score 1; 7 patients have mRS score 2; 5 patients have mRS score 3; 2 patients have mRS score 4; 1 patient have mRS score 5; 5 patients have mRS score 6. Out of the survived patients, 35 patients (70.0%) had complete recovery, while 9 patients had residual hemi paresis, 1 had dysphasia, 1 had diplopia at the time of discharge. During the follow up period 7 patients had seizure recurrence while no one had recurrent CSVT or thrombosis at other sites. 4 patients were lost to follow up during the first 3 months, 4 during the next 3 months, while 2 patients did not yet complete 6 months of follow up.

Table-2: Outcome at Discharge, 3 Months And 6 Months

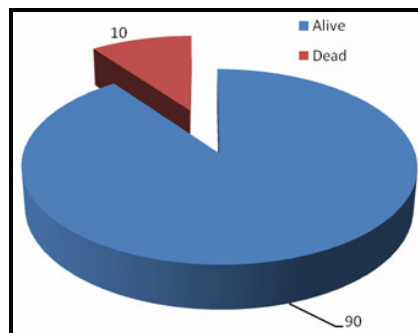
Modified rankin scale	At discharge (n=50)		3 months (n=42)		6 months (n=36)	
	No. of Cases	%	No. of Cases	%	No. of Cases	%
0	16	32.0	28	66.7	30	83.3
1	14	28.0	08	19.0	4	11.1
2	07	14.0	05	11.9	01	2.8
3	05	10.0	01	2.4	01	2.8
4	02	4.0	0	0	0	0
5	01	2.0	0	0	0	0
6(Deaths)	05	10.0	0	0	0	0

Table-3: Mortality

Status	Number of patients	Percentage
Alive	45	90
Dead	05	10
Total	50	100

In the study of 50 patients, 5 patients (10%) died and 45 patients were alive comprising (90%).

Figure-11: Pie chart showing Mortality



Discussion

In this study, totally 50 cases were studied. Comparing the age group involved, 20-40 years was the commonest age group involved in various series (Mehta SR [10] et al, 77.8% and Ameri et al [3], 61%). The present study also showed similar finding with 87.5% in the same age group, with mean age of onset 29.7 years which is comparable with Daif [11] et al (1995) 27.8%. Male to female ratio in various studies revealed, Mehta SR et al 1:1.5, Daif [11] et al (1995) is 1:1, Bousser [5-6] et al (1985) is 1.24:1. In the present study, M:F Ratio is 1:1.3. The present study is comparable to Mehta SR et al [10].

The study group consisted of 50 patients. The puerperal CVT group consisted of 27 women (54.0%) and the non-puerperal group consisted of 23 patients (46.0%) of which 4 were women and 19 were men. Nagaraj [8] et al (1987) had found that 200 out of 230 cases (86%) of CVT, seen over eight years were puerperal in nature. The experience of other authors from India had been similar like Neki NS [6] et al (2003) had found 62% of cases of CVT in postpartum period. Cantu C [7] et al from Mexico reported that obstetric CVT accounted for 59% of the cases. The present study is comparable with Neki NS [6] et al and Cantu C [7] et al.

Kurnar S [2] et al (2003) had found that 65 out of 85 cases (76%) of CVT presented with symptom duration of 4 days or less. The present study showed 70.8% of patients presented within 10 days, which is comparable with Kumar S [2] et al.

Bousser [5] et al (1985) had arbitrarily defined three main modes of onset based on the time elapsed between the appearance of the first symptom and the date of entry in hospital; acute as <48 hours, subacute as longer than 48 hours but less than one month and chronic as >1 month.

Author	Acute	Subacute	Chronic
Bousser[5] et al (1985)	36.84%	26.32%	36.84%
Daif [15]et al (1995)	35%	40%	25%
Present study (2014)	38%	46%	16%

Headache was the most common symptom in the present study accounting for 88% of patients. The present study is comparable with Daif [11] et al (1995) 82%. In the present study, 66% of cases had seizures which is comparable with Kumar S [2] et al (2003) 67%. The manifestations that indicate the cerebral cortical involvement are convulsions and paralysis, at times seizures are heralding symptoms and should arouse the suspicion of diagnosis.

In the present study, 54% of patients had focal deficits. Among them 20 had hemiparesis and 9 had dysphasia. The present study is comparable with Strolz [4] et al (2005) 56%. In the present study, 52% of patients had altered level of consciousness which is comparable with Nagaraj [8] et al (1999) and Neki S [6]et al (2003) who had 57.53% and 56% respectively. In the present study, 38% of patients had papilloedema. Similar observations were noted with Bousser [5] et al (1985) who had papilloedema in 45% of the cases.

Anemia has often been noted in 19 (38.0%) of the patients in the present study has been a hallmark in puerperal CVT. The investigative procedures like leucocyte count, blood sugar, serum creatinine, blood urea, ESR, liver function tests, serum electrolytes did not contribute to the diagnosis and were non-specific. In the present study, CSF analysis showed non-specific changes like pleocytosis (>5 cells/mm³ in 4 patients), raised proteins (>45 mg/dl in 3 patients), which did not contribute to the diagnosis of CVT. The most common finding in the present study is haemorrhagic infarction present in 56% of cases. Similar observations noted with various studies like Nagaraj [8] et al (1989), Dixit [12] et al (1997) with 40.9% and 48.4% respectively.

In the present study, the superior sagittal sinus is most commonly involved accounting for 70% followed by transverse sinus with 44% comparable with other studies like Strolz [4] et al (2005) 72.2% and Ameri [3] et al (1992) 72%. Treatment of CSVT ranges from observation to anticoagulation [12]. In our study all the 50 patients were treated with

anticoagulants, the different routes of administration reflect uncertainty of opinions among neurologists [13] as to what type of Heparin to be used. In the past CSVT had been associated with a dismal prognosis and high mortality rate, reaching 30-50% [14]. The recent ISCVT study, performed in the era of modern neuroimaging, LMWH administration and endovascular intervention, reported much lower mortality rates (8-14%) and significantly better outcome. A meta analysis of 19 studies conducted by Dertali [15] et al (2006) showed that the mortality rate during the perihospitalization period was about 5.6%, while at the end of the follow-up period, this percentage increased to 94% [15]. In patients with cerebral venous thrombosis and large parenchymal lesions causing herniation, decompressive surgery, such as craniectomy or hematoma evacuation, has been associated with improved clinical outcomes [16].

In the present study, the mean hospital stay was 12.7 days with 70% of the patients having complete recovery at the time of discharge.

Author	No. of patients (n)	Percentage (%)
Ameri [3] et al (1992)	110	5.45
Daif [15] et al (1995)	40	10
Debrujin [11] et al (2001)	59	10.17
Mehta[10] SR et al (2003)	45	4.44
Strolz [4] et al (2005)	79	15
Present study (2014)	50	10

In the present study, mortality is 10% which is comparable with Daif [11] et al (1995) and Debrujin [12] et al (2001) with 10% and 10.17% respectively.

Conclusion

- The present study emphasizes that CSVT is not an uncommon condition.
- It is an important cause of stroke especially in the peripartum settings and is one of the common causes of stroke in young.
- Clinical presentation is extremely varied and symptoms may evolve over hours to few weeks.
- Important clinical features to suggest this disorder are presentation with recent headache, seizures, papilloedema and focal deficits in the appropriate clinical settings.
- Neuroimaging plays a pivotal role in diagnosis. MRI with MRV is the current diagnostic modality of choice.
- Management with unfractionated heparin, LMWH and oral anticoagulation is appropriate. Surgical decompression is helpful in the case of continuing deterioration, inspite of maximum medical management.
- Contrary to ischemic arterial stroke, CSVT could be described as an 'all or nothing' disease with good short and long term outcomes when the acute phase of illness has been survived.

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