

# Follow Up Study (Short Term and Long Term Outcome) in Patients with Cerebral Venous Sinus Thrombosis after Treatment and Discharge from Hospital

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## ABSTRACT

**Introduction:** Study aimed to follow up the cases of cerebral venous thrombosis over short term and long term after treatment and discharge from hospital.

**Material and methods:** This prospective observational study was carried out in the department of Neurology, at Bombay hospital Indore. 75 patients included in this study, who were admitted between July 2010 to June 2013. Patients of all age groups and both sexes were included in this study. Patients were followed up to 12 months after treatment and discharge from the hospital.

**Result:** Total 75 patients were taken. M: F ratio was 1:1.4 and mean age was 36 yrs. The short term outcome and response to the treatment were good and comparable.

**Conclusion:** Overall prognosis of cerebral venous thrombosis is good in terms of recovery, low rate of neurological sequelae, low risk of recurrence and long term follow up. Chronic anticoagulant treatment is necessary to prevent recurrence of thrombosis.

**Keywords:** Cerebral Venous Sinus Thrombosis CVT, MRI, Short Term, Long Term

## INTRODUCTION

Cerebral venous thrombosis (CVT) is rare type of cerebrovascular disease associated with favourable outcome. With the help of Digital Subtraction Angiography (DSA), Magnetic Resonance Imaging (MRI) with Venography sequence leads to early diagnosis.<sup>1</sup> Incidence of CVT is approximately 3-4 cases per million per year.<sup>2</sup> Most commonly occurs in females (75%) cases. Common causes in females are oral contraceptives, pregnancy or puerperium.<sup>3-5</sup> About 25% cases are idiopathic.<sup>3</sup> Venous strokes often have a haemorrhagic component, ranging from small petechiae to an actual intracerebral haemorrhage; the latter is associated with a worse clinical outcome. The clinical presentation of CVT is highly variable ranging from mild headache or focal neurological deficits and few with seizures or coma. The best radiological examination to confirm CVT is MRI / MRV brain<sup>4</sup>, which can show evidence of sinus occlusions and parenchymal lesions. Oral anticoagulation is given for treatment and to prevent recurrences, although there is a risk of severe bleeding. Optimal duration of anticoagulation after venous thrombosis is based on the physician preference. Goal is to improve the therapeutic use of anticoagulation after the acute phase of an episode of CVT, by comparing a short term (3-6 months) versus a long term (12 months) treatment approach for the prevention of CVT recurrences.<sup>6-8</sup> The

available evidence suggests that anticoagulants are effective in reducing mortality and dependency in CVT patients; the possible role of systemic or localized thrombolysis is still to be established.

## MATERIAL AND METHODS

Prospective observational study carried out on 75 patients from July 2010 to June 2013 at Department of Neurology at Bombay hospital, Indore. MRI/MRV was done on GE MRI 1.5 tesla with phase array coil.

### Inclusion criteria

- Patients presenting with the history suggestive of cerebral venous thrombosis and confirmed by imaging of brain (MRI / MRV brain).
- Patients of all age groups irrespective of sex.
- Patients who followed up to 12 months.

### Exclusion criteria

- CT scan inconclusive of CVT
- Hypertensive hemorrhage
- Arterial stroke

Patients having claustrophobia or any metallic implants Total 75 patients were included. The diagnosis of CVT was made based on clinical and radiological features. Diagnosis of CVT confirmed by MRI combined with MR venography in all patients. We collected the demographic data; dates of onset of symptoms and signs to diagnosis; GCS score on admission and during hospitalisation; confirmation of the diagnosis by neuroimaging; location of the thrombus and sinuses involved and location of any parenchymal lesions. After confirmation of diagnosis of CVT, patients were started on anticoagulant therapy. Any bleeding tendency or contraindication to anticoagulation was ruled out in all cases before starting treatment.

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## STATISTICAL ANALYSIS

Data was entered in Microsoft excel data sheet and analysis was done by using SPSS 22.0 version software. Mean  $\pm$  SD (Min-Max) were calculated for results. Results of the cases were presented in number (percentage). Chi square test / Fisher exact test and One Sample student's t -test were the test of significance for categorical data. P value  $<$  0.05 considered as statistically significant.

## RESULTS

The patients were in the age group between 17 and 75 years, with the median age of 36 yrs. 31 males (41.3%) and 44 females (58.6%) with M: F ratio of 1:1.4

Initial treatment	No.of patients	Percentage
LMWH	50	68.5
Regular heparin	23	31.5
No anticoagulation	2	Nil

**Table-1:** Treatment during acute stage (n=73)

Short term outcome	No.of pts	Percentage	P value
Asymptomatic	36	48	0.05 (S)
Persistent diminution of vision	10	13.3	
Persistent right hemianopia	3	4	
Mild Residual weakness	13	17.3	
Persistent intermittent headache	9	12	
Death	4	5.3	

**Table-2:** Short term outcome in hospital (n=75)

Follow up	No.of pts.	Percentage	P value
Asymptomatic	28	45	0.04(S)
Persistent Focal seizure	4	6.4	
Persistent diminution of vision	10	16	
Persistent intermittent headache +diplopia	5	8	
Persistent Rt hemianopia	2	3.2	
Residual motor weakness	13	21	
Recurrence of CVT	0	nil	

**Table-3:** Follow up at the end of 1 month (n=62)

Follow up	No.of pts.	Percentage	P value
Asymptomatic	40	64.5	0.1 (NS)
Persistent diminution of vision	7	11.2	
Persistent Rt hemianopia	1	1.6	
Residual motor weakness	13	21	
Persistent intermittent headache	1	1.6	
Recurrence of CVT	0	nil	
Death	0	nil	

**Table-4:** Follow up at the end of 3 months (n=62)

Follow up 6-7 months	No of pts.	Percentage
Asymptomatic	52	92.8
Intermittent headache	1	1.9
Persistent diminution of vision	3	5.7
Recurrence of CVT	Nil	Nil
Death	Nil	Nil

**Table-5:** Follow up between 6-7 months (n=56)

## Imaging, Clinical Data, Risk Factors, Treatment

In this study, 86% patients had headache, 64% patients had vomiting and 32% patients had fever. Seizure seen in 41% of the patients. 32% patients had generalised seizures where as 5% patients had focal seizures and 4% patients had focal seizure with generalisation. 18% patients were brought in unconscious state. Papilledema was the most frequent sign in 41% patients. Motor deficit was present in 32% cases. Of these, 29% had persistent weakness and 3% had transient motor weakness (TIA). While 20% patients had altered sensorium (GCS  $<$ 8) and 3% patients were in comatose state (GCS-3). Other signs: 6<sup>th</sup> nerve palsy in 12% patients, 7<sup>th</sup> nerve palsy in 5% patients, Hemianopia in 3% patients, Occipital blindness in 1% patients, Diminished vision in 16% cases. There was evidence of mastoiditis in 3% cases and otitis media in 3% cases. Commonest MRI brain findings in our study was haemorrhagic infarcts in 44% patients while 40% patients had non-haemorrhagic infarcts. Bilateral infarcts were noted in 8% patients while 16% demonstrated no parenchymal abnormality on MRV brain.

Superior sagittal sinus (68%) was the commonest sinus to be involved followed by Transverse sinus (57.3%) and Sigmoid sinus (30.6%). Straight sinus was involved in 16% cases and cortical veins in 8% patients. Calculated P value <0.01 and it was statistically significant. There was extensive venous sinuses involvement in 10.6% cases.

About 97.3% (n=73) were put on anticoagulation treatment. 68.5% (n=50) were started on Low molecular weight heparin (LMWH) during hospitalisation. 31.5% (n=23) were started on conventional (regular) heparin -20,000 units per day during hospitalisation. Two patients (2.6%) were treated symptomatically and were not given any anticoagulation due to bleeding tendencies or associated intraventricular hemorrhage and subarachnoid hemorrhage (table-1).

Of 73 patients who received LMWH and regular heparin were switched to oral anticoagulation with warfarin/nicoumalone. PT/INR was maintained between 2-3. Prothrombin time (PT) was checked regularly during follow up. Of the 2 patients who were not given any anticoagulation, 1 patient (50%) died during hospitalisation. Among 50 patients who were treated with LMWH, 1 patient (2%) died during hospitalisation due to COPD exacerbation with type 2 respiratory failure. Among 23 patients who were treated with regular heparin, 2 patients (8.6%) died during hospitalisation because of secondary chest infection with ARDS with respiratory failure. Patients were also treated with anticonvulsants (levetericetam, phenytoin sodium, sodium valproate, carbamazepine etc.) and drugs to reduce intracranial pressure (mannitol, oral glycerol, acetazolamide and diuretics). In one patient, repeated CSF drains were done to reduce the intracranial pressure. Antibiotics were given to 4 patients initially, out of which 2 patients were suffering from mastoiditis and 2 patients were suffering from right ear otitis media. While antibiotics have been added in some patients during hospitalisation to prevent secondary chest infections, catheter associated infections, diarrhoea and other hospital acquired infections.

#### Short term outcome (in hospital)

During hospitalisation, the mortality was 5.3% (n=4). Among the remaining 71 patients, 10 patients (13.3%) were having persistent diminution of vision and 3 patients (4%) were having right hemianopia. 13 patients (17.3%) were having mild residual weakness on hemiplegic side and 9 patients (12%) had persistent intermittent headache. Rest 36 patients (48%) were asymptomatic at the time of discharge (table-2).

#### Follow up at the end of 1 month

Among 71 patients, 62 patients (87.5%) were followed up post discharge. 9 patients were lost to follow up. Of these 62 patients, 4 patients (6.4%) have persistent recurrent focal seizures but less frequent. 10 patients (16%) had persistent diminution of vision because of secondary optic atrophy (secondary to papilledema). 5 patients (8%) had persistent intermittent headache and diplopia. The residual motor weakness of 13 patients (21%) improved gradually on follow up after 1 month. The rest of 28 patients (45%) remained

asymptomatic (table-3).

#### Follow up at the end of 3 months: (n=62)

All the 62 patients were followed up after 3 months. Of these 62 patients, only 7 patients (11.2%) had persistent diminution of vision due to secondary optic atrophy. Only 1.6% patient (n=1) had persistent right hemianopia. 1.6% patient (n=1) had persistent intermittent headache and diplopia. Fundus examination of that patient revealed papilledema. Therefore, this patient was readmitted and a thecoperitoneal shunt was put, after which the patient improved. The motor power of remaining 13 patients (21%) were gradually improved. Rest of remaining 40 patients (64.5%) remained asymptomatic (table-4).

Follow up of MRI and MRV was done in 62 patients at the end of 3 months. Following were the findings:

MRV of 2 patients showed no recanalization but there were development of collaterals. As the patients remained asymptomatic, they were continued with oral anticoagulants. In all other patients, MRV revealed partial recanalization of the thrombosed sinuses, collaterals formation and partial resolution of parenchymal lesions.

#### Follow up between 6 -7 months: (n=56)

56 patients were followed up between 6-7 months. Six patients were lost to follow up. One patient (1.9%) had persistent intermittent headache. Vision remained diminished in 3 patients (5.7%) with secondary optic atrophy. In the patients with right hemianopia, the field defect improved. All the other 52 patients (92.8%) remained asymptomatic at the end of 6-7 months (table-5).

MRI and MRV was done in 56 patients between 6-7 months of follow up:

All the patients had complete resolution of the parenchymal lesions on MRI and MRV. In one patient, there was no evidence of recanalization but there was good collateral circulation. In one patient, there was partial recanalization and in rest of the patients, there was complete recanalization of the thrombosed sinuses.

#### Long term outcome at 12 months: (n=54)

Up to 12 months, total 54 patients were followed up. Two patients were lost to follow up. Four patients has stopped anticoagulants on their own. Those patients were asymptomatic; hence, they were not restarted on anticoagulants. All the other patients (94.5%) were taking oral anticoagulants and were asymptomatic except for 3 patients (5.5%) with diminished vision secondary to optic atrophy (table-6).

At the end of 1 year, MRI was repeated in the following patients:

#### MRI changes at the end of 12 months

MRI changes	No.of pts	Percentage
No recanalization	Nil	Nil
Partial recanalization	1	1.9
Complete recanalization	53	98.1
Collaterals	54	100
Resolution of parenchymal lesion	54	100



Recurrence	Nil	Nil
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MRV done in all 54 patients after the end of 1 year. Only 1 patient (1.9%) showed evidence of partial recanalization while in rest all other 53 patients (98.1%) showed complete recanalization. In all patients, there were collaterals formation and resolution of parenchymal lesions. There were no recurrence of cerebral venous sinus thrombosis in any of these patients.

Following is the summary of the long term outcome in the 54 patients followed up in the study:

Long Term outcome (at the end of 1 year)	No.of pts	Percentage
Complete recovery	51	94.5
Residual deficit	3	5.5
Recurrence of CVT	Nil	Nil
Death	Nil	Nil

**Total mortality rates:** In our study, during hospitalisation among 75 cases, only 4 patients died.

## DISCUSSION

In this study, M: F was 1:1.4 and the mean age of patients was 36 years. Use of oral contraceptive drugs was related to CVT in 13.3% patients (n=10), indicating that it is an important etiological factor responsible for CVT in young females. Puerperium was the most common risk factor associated with CVT in pregnant females. 2 patients with mastoiditis and 2 patients of otitis media diagnosed with CVT, suggesting that infection as the etiological factor responsible in those cases. Headache was the commonest symptom (86%) cases with vomiting (64%) cases. Seizures were present in 41% cases. Papilledema was the most common presenting sign in 41% patients. Motor deficit in 32% cases while altered sensorium present in 20% cases. MRI and MRV are more sensitive in diagnosing CVT than CT scan. On MRI/MRV study during the acute stage, superior sagittal sinus 68% was the most commonly involved sinus followed by transverse sinus 57.3% and sigmoid sinus 30.6%. While there were extensive venous sinus thrombosis in 10.6% cases.

Low molecular weight heparin (68.5%) was used in more number of patients than regular heparin (31.5%) during the acute stage. We preferred LMWH in our patients because of less risk of bleeding, ease of administration, less chance of thrombocytopenia, does not require monitoring. Short term outcome and response of both the treatment were good and comparable. Of the 75 patients, 4 died during hospitalisation. Among the remaining 71 patients, 10 patients were having persistent diminution of vision and 3 patients were having right hemianopia. 23 patients were having residual motor weakness and 9 patients had persistent intermittent headache. Rest other 26 patients were asymptomatic at the time of discharge.

At the end of 1 month, 9 patients were lost to follow up. Of 62 patients, 4 patients have persistent recurrent focal seizures. 10 patients had diminution of vision. 5 patients had persistent intermittent headache and diplopia. Residual motor weakness of 13 patients improved gradually on follow up. Rest 28

patients remained asymptomatic. At the end of 3 months, among 62 patients, only 7 patient had persistent diminution of vision. Only 1 patient had persistent right hemianopia. 1 patient had persistent intermittent headache and diplopia. The motor power of remaining 13 patients were gradually improved. Rest 40 patients remained asymptomatic. MRV done in 62 patients showed development of collaterals (100%), 60 patients (96.8%) showed evidence of partial recanalization while in 2 patients (3.2%) there were no recanalization of thrombosed sinuses.

Long term outcome between 6-7 months, 6 patients were lost to follow up. Among 56 patients, 1 patient had persistent intermittent headache. Vision remained diminished in 3 patients with secondary optic atrophy. In the patients with right hemianopia, the field defect improved. All the other 52 patients remained asymptomatic at the end of 6-7 months. Follow up MRI/MRV (n=56) revealed complete recanalization in 96.4% patients (n=54) complete recanalization with reduction in calibre of sinuses in 96.4% patients (n=54) and partial recanalization in 1.8% patient (n=1) while 1.8% patient (n=1) had no recanalization in thrombosed sinuses.

Long term follow up at the end of 12 months, two patients were lost to follow up. Out of 54 patients, 51 patients (94.5%) remained asymptomatic while 3 patients (5.5%) had persistent diminished vision secondary to optic atrophy. There was no recurrence of cerebral venous sinus thrombosis in any of the patients. There was no recurrence of seizures in the patients who were on anticonvulsants after the acute thrombosis. Anticonvulsants were given for a mean duration of 3 years in our patients.

## CONCLUSION

With the use of MRI/MRV helps in early diagnosis of CVT. Overall prognosis of CVT is good in terms of recovery, low rate of neurological sequelae and low risk of recurrence. Short term and long term outcome are very good with treatment in CVT patients. Patient should be treated adequately with anticoagulants, anticonvulsants, antiedema measures during the acute stage. Chronic anticoagulant treatment is necessary to prevent recurrence of thrombosis.

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