ABSTRACT
Introduction: Cerebral venous thrombosis (thrombosis of cerebral veins and sinuses) accounting for 0.5% of all strokes has a variable clinical presentation making early diagnosis difficult. A number of prothrombotic states have been implicated in causation of cerebral venous sinus thrombosis. Anticoagulation with intravenous heparin followed by warfarin for 3-6 months is currently recommended for majority of cases, even in the presence of mild or moderate hemorrhagic transformation. This may need to be continued for longer in some patients who have underlying prothrombotic states.

Aim: To study clinical profile and outcome of patients of cerebral venous sinus thrombosis admitted in a tertiary care hospital in northern India.

Materials and Methods: The study was carried out in a tertiary care hospital where all patients of cerebral venous thrombosis admitted between 1st January 2005 and 31st December, 2008 (retrospective) and between 1st January 2009 and 30th June 2010 (prospective) were included in the study. The enrolled patients were studied for their demographic profile and complete history was taken. Patients were followed up for minimum period of 6 months and outcome was assessed on basis of morbidity and mortality on follow-up.

Results: A total of 46 patients of cerebral venous sinus thrombosis were included in the study. The mean age of the patients was 35.5 years. Out of 25 female patients in the study group, 8 female patients (32%) had puerperium as risk factor and 4 patients (16%) had oral contraceptive use as risk factor. Most common symptom was headache which was present in 41 patients comprising 89.1% of total patients. 39 patients (84.8%) were alive at the end of follow-up and 7 patients died (15.2%). 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: The recent advances in early diagnosis and prompt management of cerebral venous thrombosis have significantly improved its outcome with markedly decreased morbidity and mortality. The role of endovascular thrombolysis and decompressive craniectomy in the management of severe cerebral venous thrombosis cases remain to be defined. Cerebral venous sinus thrombosis is a clinical entity with a low risk of death and good long-term prognosis in modern era.

Keywords: Anticoagulation, Prothrombotic, Stroke

INTRODUCTION
Thrombosis of cerebral veins and/or sinuses constitutes a rare clinical entity. It usually affects young individuals. Cerebral venous thrombosis can be caused by a number of prothrombotic states (congenital or acquired) such as deficiencies in anticoagulation-promoting proteins, usage of oral contraceptives, pregnancy, dehydration, trauma, inflammatory diseases, infections and hematological conditions. The presenting clinical picture of cerebral venous thrombosis is non-specific, may vary significantly which makes the diagnosis of cerebral venous thrombosis quite puzzling. Cerebral venous sinus thrombosis may be encountered not only by neurologists and neurosurgeons but also by emergency physicians, oncologists, hematologists, obstetricians, pediatricians, and family practitioners due to diversity of causes and presenting scenarios [1].

Maintaining a high degree of clinical suspicion in the setting of common presenting symptoms helps in early diagnosis of venous sinus thrombosis. Clinical findings are related to increased intracranial pressure attributable to impaired venous drainage and to focal brain injury from venous infarction or haemorrhage. Most common finding in cerebral venous sinus thrombosis includes focal neurological signs (including focal seizures) [2]. Various laboratory studies along with Magnetic Resonance Imaging and Magnetic Resonance Venography are necessary for establishing a diagnosis. Treatment involves
anticoagulation with unfractionated heparin or low molecular heparin, even if intracranial haemorrhage is present [3]. The aim of the study was to study clinical profile and outcome of patients of cerebral venous sinus thrombosis admitted in a tertiary care hospital in northern India.

MATERIALS AND METHODS
A total of 46 patients of cerebral venous sinus thrombosis presenting in a tertiary care hospital in Northern India from 1st January 2005 to 31st December 2008 (retrospective) and between 1st January 2009 and 30th June 2010 (prospective) were included in the study. The study was approved by the ethics committee and an informed consent was taken by all the enrolled patients.

All patients aged above 18 years with one and/or more clinical features consistent with cerebral venous sinus thrombosis like seizures, headache, papilledema, focal neurological deficit, altered sensorium and with evidence of venous sinus thrombosis on Magnetic Resonance Venography were included in the study. All patients with incomplete clinical or radiological record, inconclusive radiological studies and cavernous sinus thrombosis 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 subacute, and patients with onset more than one month were considered chronic.

The enrolled patients were studied for their demographic profile and complete history was taken. 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, Magnetic Resonance Venography, CT angiography, and Protein C, Protein S, Antithrombin III, Homocysteine levels, Factor V Leiden and Anticardiolipin antibodies wherever possible. All patients were treated with intravenous heparin at the time of admission followed by overlap with oral anticoagulant which was continued for minimum period of six months. Decompressive craniotomy was performed in two cases to reduce intracranial hypertension.

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 [Table/Fig-1] at time of discharge and follow-up [4]. Patients were categorized as having no disability, mild disability, moderate disability and severe disability on basis of Rankin disability score. At the end of follow-up, patients were also assessed for persistence of headache, focal neurological deficit and recurrence of seizures.

RESULTS
Out of 46 patients in study group, 67.4% of the patients (31 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. 25 patients were female (54.3%) and 21 (45.6%) were male. Out of 25 female patients in the study group, 8 female patients (32%) had puerperium as risk factor and 4 patients (16%) had oral contraceptive use as risk factor [Table/Fig-2]. Ulcerative colitis and subsequent corticosteroid use was found as predisposing factor in one male patient (2.1%). M astoiditis was noted in one female patient (2.1%). Protein C, Protein S and Antithrombin III were carried out in only seven patients and out of them three had protein S deficiency, one had protein C deficiency and one had deficiency of all these three proteins.

In present study, 16 patients presented within 48 hours of onset of symptoms comprising 34.8% of total population in the study group. 28 patients presented within 48 hours to one month of onset of symptoms constituting 60.9% of total population in study group and two patients presented after one month of onset of symptoms comprising 4.3% of total patients. Assessment of symptoms showed that the most common symptom was headache which was present in 41 patients comprising 89.1% of total patients. Convulsions were present in 24 patients constituting 52.1% of total patients in the study group and focal deficits were seen in 22 patients constituting 47.8% of total patients [Table/Fig-3].

Altered sensorium at the time of admission was present in 43.5% of patients (20 cases). 23 patients (50%) had papilledema and 12 patients (26.1%) had hemiparesis in the study group. Two patients had monoparesis and one patient had quadriparesis at the time of admission. Four patients (8.7%) had cranial nerve paralysis, out of which three had

| Rankin = 0 | No symptoms at all |
| Rankin = 1 | No significant disability symptoms, able to carry out all usual activities and duties |
| Rankin = 2 | Slight disability. Unable to carry out normal activities but able to look after own affairs without assistance |
| Rankin = 3 | Moderate disability requiring some help but able to walk without assistance |
| Rankin = 4 | Moderate severe disability. Unable to walk without assistance, and unable to attend to own bodily needs without assistance |
| Rankin = 5 | Severe disability. Bedridden, incontinent and requiring constant nursing care and attention |

[Table/Fig-1]: Rankin disability score
Magnetic Resonance Imaging of brain showed that out of 46 patients, 26 patients (56.5%) had hemorrhagic infarction while 20 patients had (43.5%) had non-hemorrhagic infarction. Mass effect was seen in 5 patients accounting for 10.8% of all patients and bilateral infarct was seen in 4 patients comprising 8.7% of all patients. Superior sagittal sinus was most commonly involved (67.4%). The left transverse sinus was involved in 19 patients (41.3%) and left sigmoid sinus in 14 patients (30.4%). The other sinuses involved included right transverse sinus in 11 (23.9%), right sigmoid sinus in 7 (15.2%), jugular sinus in 4 (8.7%), straight sinus in 3 (6.5%), cortical vein in 2 (4.3%) and internal cerebral vein in 1 (2.1%).

In this study, at the time of discharge 23 patients (50% patients) had Rankin disability score of 0 and 1 and thus no disability. Eleven patients had Rankin disability score of 2 hence falling into mild disability group and six patients had Rankin disability score of 3-4, hence falling into moderate disability group. This accounts for 13% of all patients. None of the patients had a severe disability at the time of discharge. At the time of discharge 40 patients were alive (87%) and six patients died (13%). Out of 25 female patients, three died at the time of discharge accounting for 12% of total females in study group. Out of 21 male patients, three died accounting for 14.3% of total male patients in the study group.

One patient had died during six months of follow-up and 39 patients were alive at the end of six months. Nine patients had headache on follow-up accounting for 19.5% of total patients. Focal neurological deficit persisted in seven patients accounting for 15.2% and convulsions occurred in four patients on follow up accounting for 8.6%. On follow-up out of 39 patients, 31 cases (79%) had no disability symptoms, five patients had mild disability (13%) and three patients had moderate disability.

DISCUSSION

Cerebral venous thrombosis accounts for 0.5% of all stroke [5]. Cerebral venous sinus thrombosis may result from extrinsic compression or partially obstructing thrombus that may progress to completely occlude the sinus. Strokes resulting from cerebral venous sinus thrombosis have distinct clinical profile, usually affecting young persons, predominantly women and carry a significant mortality if not adequately treated. Highest frequency of cerebral venous sinus thrombosis is seen in patients with age between 20-40 years [6]. 67.4% of patients were in the age group 19-40 years in our study. Incidence was more common in females than male which was comparable to other studies.

Although cerebral venous sinus thrombosis may affect people of all age groups but young women are slightly more susceptible because of specific causes like oral contraceptives, pregnancy and puerperium. Venous thrombosis can be caused by number of prothrombotic states and disorders of the clotting system like factor V Leiden mutation, protein C and protein S resistance, prothrombin gene abnormalities and anti-thrombin III deficiency. Acquired abnormalities associated with cerebral venous sinus thrombosis include antiphospholipid antibodies, malignancy, dehydration, infection, hematological conditions, inflammatory systemic conditions, trauma, post operative infections and operative procedures.

In the present study, 32 % of females (8 patients) were identified to have puerperium as a risk factor and oral contraceptives use as a risk factor was present in 16% of females (4 females). Pillai et al., in a study found out use of oral contraceptive pills as risk factor in 38.4% cases and puerperium in 23% cases [7].

One patient had ulcerative colitis and steroid use as risk factor in our study. One patient (2.1%) had mastoiditis as risk factor for vertebral venous sinus thrombosis. Daif et al., reported infection in 7% of cases as risk factor for cerebral venous sinus thrombosis in his study [8]. Incidence of cerebral venous sinus thrombosis after infection has decreased significantly in the modern era with advent of antibiotics. No obvious risk factor was found in 32 patients (69.6%) in the study group.

Impact of cerebral venous sinus thrombosis may vary from completely normal parenchyma to brain edema and / or haemorrhage. Non-specific clinical presentation may sometimes lead to delay in making a diagnosis. If disease is restricted to dural sinus, it may present with symptoms of raised intracranial pressure while if cortical veins are involved, focal deficits and convulsions may be the presenting features. Headache was the most common symptom in the present study accounting for 89.1% patients. In international study on cerebral venous sinus thrombosis, headache was the most common symptom and was present in 89% of patients.
In present study, 43.5% of patients had altered level of consciousness which is comparable with Stolz et al., who reported 36.7% with altered sensorium [9]. In our study 15.2% patients (seven patients) died at end of study period and all of them had altered sensorium at the time of presentation. Seizures at times may herald symptoms and should arouse the suspicion of cortical involvement in cerebral venous sinus thrombosis. In present study, 52% of cases had seizures while Mangshetty et al., reported 66% incidence of seizures in cerebral venous sinus thrombosis [10]. Factors associated with increased frequency of epileptic episodes include parenchymal involvement and presence of focal neurological deficits [11].

About half of patients with cerebral venous sinus thrombosis develop cerebral parenchymal lesions and neurological signs [12]. In the present study, 47.8% patients had focal deficits (paresis in 36.9%). Presence of focal neurological deficit at time of admission was associated with increased morbidity and mortality on follow up.

Computed tomography of the brain with or without contrast is usually the first investigation to be carried out and is useful in showing brain or sinus changes suggestive of cerebral venous sinus thrombosis. The current practice is to use Magnetic Resonance Venography with Magnetic Resonance Imaging head for diagnosis. Haemorrhagic infarction mainly affects cortex and adjacent white matter and occurs in approximately 10-50% of cases [13]. In present study, haemorrhagic infarction was present in 56.5% of cases and haemorrhagic infarction was present in 43.5% cases. Thrombosis usually affects (in order of decreasing frequency) the superior sagittal sinus, lateral sinus and cavernous sinus. In present study, superior sagittal sinus was involved in 67.4% cases.

In present study at the end of follow-up 31 patients (67.4%) had no disability, five patients (10.9%) had mild disability and three patients (6.5%) had moderate disability symptoms. None of the patients had severe disability symptoms. Recurrence was seen in 2.1% patients. Mortality rate in present study group was 15.2%.

Treatment involves identification and removal of precipitating factor. Anticoagulation improves outcome even in patients with hemorrhage on Computed Tomography. Once symptomatic improvement occurs, heparin is replaced with oral anticoagulation with aim to adjust International Normalized Ratio between two and three. Treatment with intravenous thrombolytic agents or direct endovascular thrombolytic agents is advocated in patients when medical therapy fails but carries risk of hemorrhage. Various methods are used to reduce intracranial hypertension like steroids, mannitol, glycerol, acetazolamide, shunting or even surgical decompression.

Cerebral venous sinus thrombosis had been associated with a dismal prognosis and high mortality rate of up to 30-50% in the past [14]. Recent studies report better outcome with much lower mortality rates. In this study, complete or partial recovery was observed in approximately 78% of patients, whereas 6.5% had poor outcome with permanent neurological deficits and with mortality rate of around 15%. Dentali et al., in his meta-analysis of 19 studies showed that mortality rate during peri-hospitalization period was about 5.6% while at the end of follow-up period it was 9.4% [15].

**CONCLUSION**

The present study emphasizes that cerebral venous sinus thrombosis is an important cause of stroke especially in the peripartum settings and in the young. The spectrum of clinical presentation is extremely wide and non-specific making diagnosis difficult. Treatment follows the directions of identification and elimination of underlying cause, management of intracranial hypertension, anticoagulation administration and anticonvulsive treatment.

**REFERENCES**


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