SAS Journal of Medicine ISSN 2454-5112
SAS J. Med., Volume-3; Issue-7 (Jul, 2017); p-140-146
Available online at http://sassociety.com/sasjm/

Original Research Article

Clinical Profile of Cerebral Venous Thrombosis: Cases Admitted to HSK Hospital Bagalkot

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Abstract: Cerebral venous thrombosis (CVT) is an uncommon cause of stroke with wide variety of clinical presentations, etiological factors, imaging findings, and outcomes, and thus can be extremely challenging to diagnose. CSVT represents almost 0.5-3% of all stroke. The early diagnosis of CVT is crucial because timely and appropriate therapy can reverse the disease process and significantly reduce the risk of acute complications and long-term squeal . In this article, we have reviewed the epidemiology, causative factors, clinical features, diagnosis and treatment of CVT patients admitted in neurology department in HSK hospital, Bagalkot.
Keywords: Cerebral venous thrombosis (CVT), epidemiology, causative factors, clinical.

INTRODUCTION

Cerebral venous /sinus Thrombosis (CVT) has been recognized since the early 19th century but still it remains a diagnostic and therapeutic challenge.

The first description of CVT, appearing in the French literature in 1825, was by Ribes, in a 45-year old man who died after a 6-month history of severe headache, epilepsy, and delirium[1]. In 1957, Padmavati *et al.*, for the first time from India, reported 15 cases of CVT in puerperium in an epidemiological study evaluating the causes of hemiplegia in 44 women[2].

It was at that time recognized as a diagnosis which was mostly made at autopsy and considered lethal. With the advent of newer and more sophisticated imaging techniques and increasing awareness of this entity, the incidence of this disease has increased and the prognosis has improved as compared to the older series.

Cerebral vein and sinus thrombosis is rare compared to arterial stroke often occurs in young individuals. CVT may occur at any time from infancy to old age most reported cases were women in association with puerperium.

Onset of symptoms may be acute sub-acute or chronic. Cerebral venous infarction and hemorrhagic transformation is the most serious consequence of cerebral venous thrombosis venous infarctions are often multifocal bilateral affecting both grey matter and sub cortical white matter depending of sinus involved.

Aims and objective

We undertook this study to determine the frequency, clinical patterns, and aetiologies of cerebral venous thrombosis of all the patients presenting to our hospital.

MATERIALS AND METHODS

It was a retrospective study based on the Records of all adult aged 18 years and old, admitted and documented with diagnosis of cerebral venous thrombosis from Nov 2014 through Dec 2016 in, HSK hospital, Bagalkot.

Inclusion Criteria

- All the patients admitted to HSK hospital with neuroimaging diagnosis of CVT were included in the study .

Exclusion Criteria

Cases of cerebrovascular accident other than cvt such as arterial stroke were excluded from our study.

RESULTS

Demographic Profile

The mean age of patients in the large studies published from India ranged from 31.3 to 48.7 years. In the largest hospital−based prospective cohort study from India (Nizam's Institute Venous Stroke Registry

[NIVSR]) by Narayan *et al.*, 428 consecutive patients with CVT were enrolled over a period of 8 years from a tertiary care hospital from South India, the mean age of the patients in this study being 31.3 years[3].

Most of the earlier case series from india reported a higher proportion of women suffering from CVT this gender bias was usually attributed to gender specific risk factor like usage of oral contraceptive, puerperium and pregnancy. One large prospective study which recruited 612 consecutive patients of CVT from various hospitals of Mumbai had male to female ratio of 3:2 determing the better obstetric care.

A total of 100 cases of CVT were admitted from emergency department of HSK hospital Among CVT patients (49 women, 41men) aged 15 to 45 years were identified and only (6 men, 4 women) were of older age group.

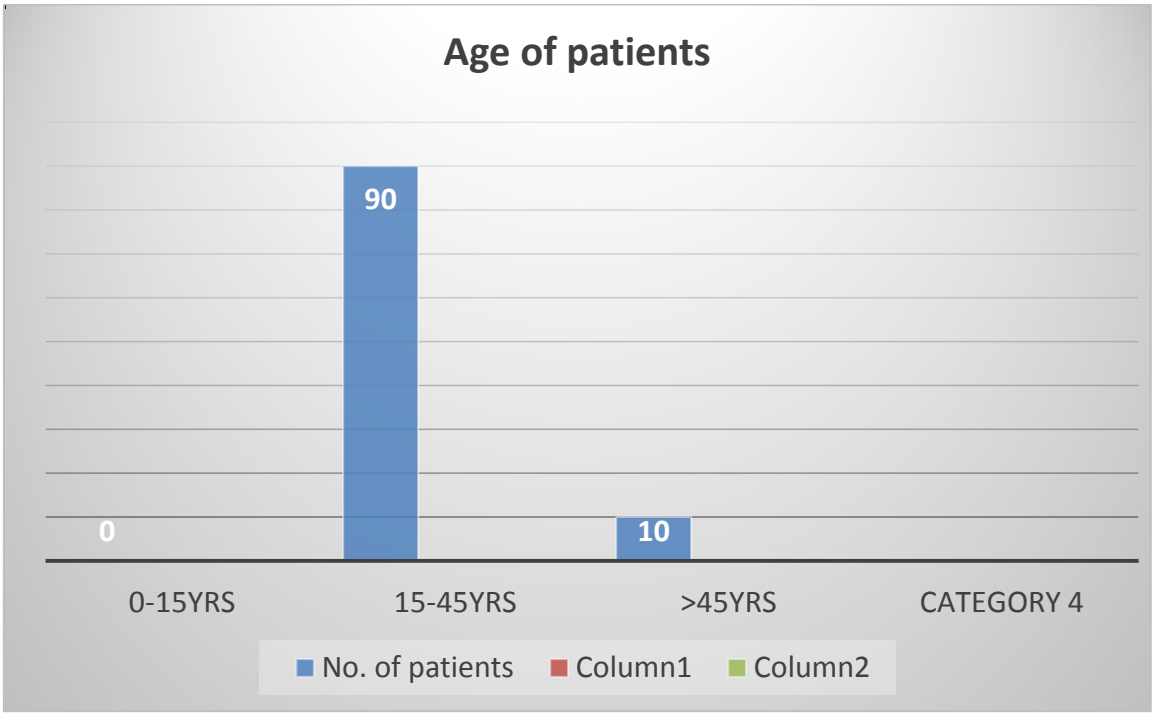

Fig-1: Age of patients

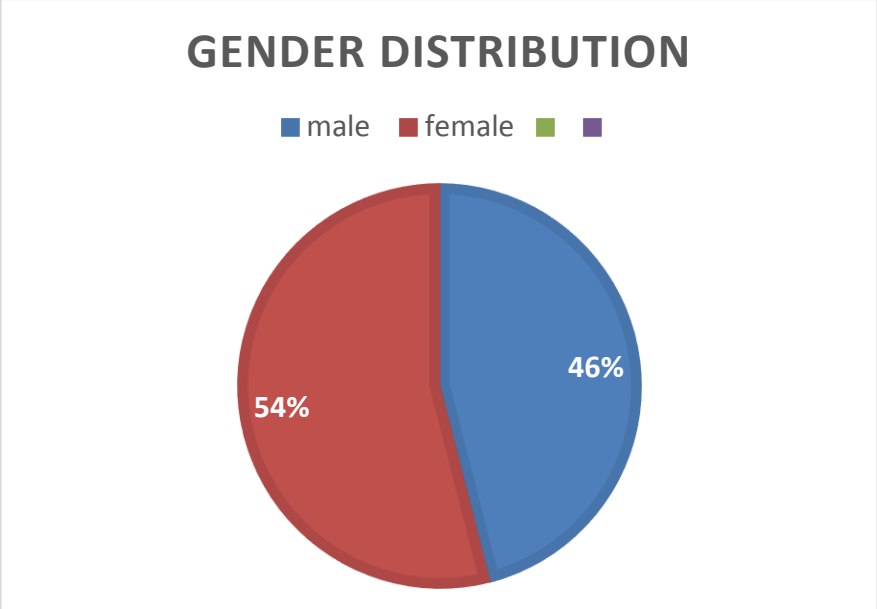

Fig-2: Gender distribution

Etiological factors

More than 100 causes of CVT have been described in the literature . The risk factors for venous thrombosis, in general, are linked classically to the Virchow triad of stasis of the blood, changes in the vessel wall, and changes in the composition of blood. Etiological factors are usually divided into acquired risks (e.g. surgery, trauma, pregnancy, puerperium, antiphospholipid syndrome, cancer, exogenous hormones) and genetic risks (inherited thrombophilia). Drugs like oral contraceptives (OCs), steroids, hormone replacement therapy, and oncological treatments have been implicated in the causation of CVT.

A total of 46 cases were found to be in Puerperium and pregnancy, which is found to be the the most common predisposing factors for CVT . Most of the pregnancy−related CVT occurs in the third trimester or puerperium. During pregnancy and for 6–8 weeks after birth, women are at increased risk of developing venous thromboembolic (VTE) events. Pregnancy induces several prothrombotic changes in the coagulation system that persists at least during early puerperium. Hypercoagulability worsens after delivery as a result of volume depletion and trauma. Most of the earlier case series of CVT reported from India have very high proportions of puerperal CVT. In 1984, Srinivasan, reported 135 cases of stroke in women, of whom only 6 had an arterial stroke, and the rest had a CVT.

While another common cause less identified is chronic alcoholic patients in our study we found 26 cases , though the pathophysiology of alcohol consumption causing stroke has not been completely explained, various mechanism such as induction of cardiac arrhythmias and cardiac wall motion abnormalities, induction of hypertension, enhancement of platelet aggregation and activation of the clotting cascade and reduction of cerebral blood flow by cerebral vascular smooth muscle contraction have been proposed[4].

We also found higher rate of HIV patients presenting with CVT in which 6 out of 9 initial presentation was CVT and on routine investigation was found to HIV positive while 3 patients were already on A.R.T . opportunistic infection were ruled out in all the patients. Mechanisms for the observed hypercoagulability in HIV infected patients are multifactorial and include the presence of antiphospholipid antibodies and deficiency of natural anticoagulants such as protein C, protein S, heparin cofactor II, and antithrombin[5]. Some studies have reported a high prevalence of antibodies against protein S among HIV infected patients, leading to significantly low protein S activity in about 31%-76% of patients .

Now compared to other western studies having high incidence of CVT in the OCP users in our study we found 10 patients with oral contraceptives use. Hormonal contraception is used by more than 100 million women throughout the world. Shortly after its introduction in the 1960s oral contraception (OC) was linked to an increased incidence of thrombovascular disease. This is mediated by its effects on the haemostatic system. Procoagulation activity caused by increased activity of coagulation factors VII, X and fibrinogen is a common finding in almost all preparations[6].

In our study

1. Pregnancy and puerperium in 46 cases
2. Heavy alcohol consumption (>160gm/day) and chronic Alcoholics was present in 16 cases,
3. Acute gastroenteritis patients in 10 cases ,
4. antiphospholipid antibodies in 4 cases,
5. oral contraceptives and hormonal pills(OCP) in 10,
6. otitis media in 3,
7. leukaemia in 2 ,
8. HIV in 9 and
9. Factor V Leiden in one case .

Clinical Presentation

Cerebral venous thrombosis (CVT) is an under diagnosed condition for acute or slowly progressive neurological deficit. CVT is less frequent than arterial thrombosis. CVT has a wide spectrum of signs and symptoms, which may evolve suddenly or over the weeks. It is clinically challenging and mimics many neurological conditions such as meningitis, encephalopathy, benign intracranial hypertension, and stroke[7].With increasing awareness, CVT cases are now being diagnosed more frequently. Headache is the most frequent symptom in patients with CVT, present in about 80% of cases. However, headache presenting as the only symptom of CVT is rare and it is usually seen in combination with other neurological signs and symptoms (seizures, focal neurological deficit and signs of intracranial hypertension) [8]. Clinical findings in CVT fall into two major categories.

Those related to increased intracranial pressure due to impaired venous drainage; and, those related to focal brain injury from venous ischemia/infarction or haemorrhagic transformation.

Type	Duration	Frequency
Acute	< 48 hours	30%
Sub-acute	48 hours – 30 days	50%
Chronic	30 days – 6 months	20%

Fig-3: Type of CVR

Most of the patients presented in the sub acute stage 50% of the patients while 30% of patients in the acute state <48hours while only 20% of patients presented in chronic stage more then 30 days.

CVT PATIENT NEUROIMAGING

Noncontrast computed tomography is usually the first-choice examination in the diagnostics of acute CNS disorders. Hyperdensity of dural sinus , cortical vein (cord sign) or deep veins is characteristic for CVT due to increased density of thrombus in comparison with the flowing blood . These symptoms may sometimes coexist. One should remember that hyperdensity of dural sinuses or cerebral veins may be also seen in dehydration or with elevated hematocrit. Transverse sinus thrombosis may be also mimicked by blood layered on cerebellar tentorium in a course of acute subdural hemorrhage or by epidural hematoma at the level of the sinus. Unfortunately, sensitivity of this method is relatively low and it is estimated that thrombosis may be visualized in about 1/3 of cases, while in the remaining cases cerebral image is unremarkable . Therefore, in patients with clinical suspicion of CVT or those with ambiguous results of initial CT imaging the diagnostics should be broadened to include CT venography or MRI venography was performed[9].

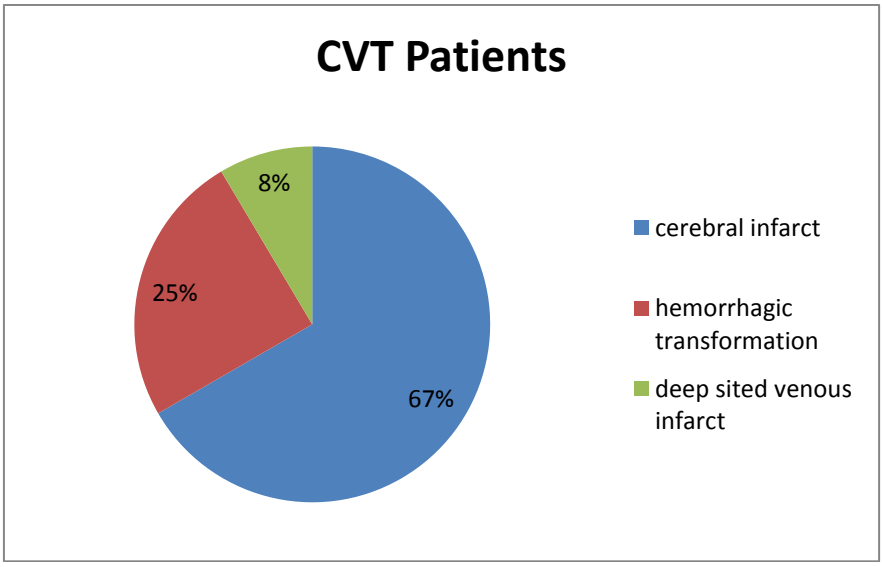

Fig-4: CVT Patients

In our study most of the patients 67%of patients had cerebral infarct ,while around 25%of patients had haemorrhagic infarct and deep sited venous infarct in 8% of patients.

Sinus thrombosis location

Superior sagittal sinus was involved in 78 patients, (isolated SSS in 7 pts). Transverse sinus was involved 66 pts, (isolated in 4pts) followed by sigmoid sinus 44 pts . Superficial and deep venous system was involved in 10pts. Majority (78 pts) of patients had combination of sinuses and veins involvement , 11 pts had only isolated sinus involvement .

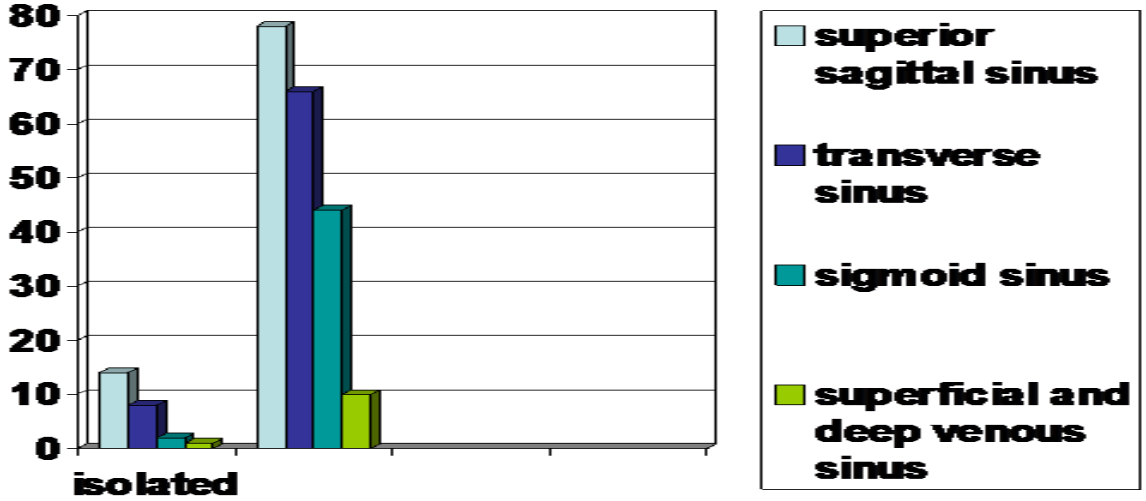

Fig-5: Sinus thrombosis location

Sign and Symptoms

To understand the symptoms and signs of sinus thrombosis, two different mechanisms should be distinguished: thrombosis of the cerebral veins, with local effects caused by venous obstruction, and thrombosis of the major sinuses, which causes intracranial hypertension.

In the majority of patients, these two processes occur simultaneously. The first mechanism, occlusion of the cerebral veins, can cause localized oedema of the brain and venous infarction. Pathological examination shows enlarged, swollen veins, oedema, ischaemic neuronal damage, and petechial haemorrhages. Two different kinds of cerebral oedema can develop. Cytotoxic oedema is caused by ischaemia, which damages the energy-dependent cellular membrane pumps, leading to intracellular swelling. The second type, vasogenic oedema, is caused by a disruption in the blood-brain barrier and leakage of blood plasma into the interstitial space. The second mechanism leads to the development of intracranial hypertension as a result of occlusion of the major venous sinuses.

Normally, the cerebrospinal fluid is transported from the cerebral ventricles through the subarachnoid spaces at the base and surface of the brain to the arachnoid villi, where it is absorbed and drained into the superior sagittal sinus. Thrombosis of the sinuses leads to increased venous pressure, impaired absorption of cerebrospinal fluid, and consequently, increased intracranial pressure. The obstruction to the drainage of cerebrospinal fluid is located at the end of its transport pathway, and no pressure gradient develops between the subarachnoid spaces at the surface of the brain and the ventricles. Hence, the ventricles do not dilate, and hydrocephalus does not normally complicate venous sinus thrombosis. About one fifth of patients with venous sinus thrombosis have intracranial hypertension only, without signs of cortical vein thrombosis[10].

•Headache is the most frequent and most of the times, the earliest symptom of CVT in 90% of cases.
•Seizures in 40% of cases and more common in per partum CVT causing 70% of cases.
•Other symptoms include paresis (37.2%); papilledema (28.3%); altered mental state (22%), aphasia (19.1%), stupor or coma (13.9%), diplopia (13.5%), and visual deficits (13.2%).

Diagnosis

In our study all the patients presented to us with manifestation suggestive of CVST underwent CT scan, MRI BRAIN with MRV and was confirmed to have the diagnosis of CSVT. History and Routine blood studies consisting of a complete blood count, chemistry panel, prothrombin time, and activated partialthromboplastin time (PTT) are recommended for patients with suspected CVT. The results from these tests may suggest the presence of conditions that contribute to the development of CVT such as an underlying hypercoagulable state, an infection, or an inflammatory process. Screening for potential prothrombotic conditions that may predispose to CVT is recommended helped us to identify the likely aetiology leading to CSVT.

Management

The immediate goals of anticoagulant (AC) therapy are to recanalize the occluded sinus, prevent propagation of the thrombus and to treat the underlying prothrombotic state. Heparin is the obvious therapy for any venous thrombosis yet AC therapy has been controversial, due to the high incidence of spontaneous haemorrhagic infarcts in patients with CVT.

Guidelines from India, Europe and America recommend that patients with CVT without contraindications for AC should be treated either with

activated partial thromboplastin time adjusted IV heparin or body−weight−adjusted LMWH.

The presence of concomitant intra−cranial hemorrhage related to CVT is not a contraindication for heparin therapy. The optimal duration of heparin is not established. As for deep vein thrombosis of the leg, after a few days of heparin, once the patient is stabilized, oral ACs are started to reduce the risk of heparin−induced thrombocytopenia.
Warfarin is usually adjusted to obtain an International Normalized Ratio between 2 and 3. The usually recommended duration of treatment is 3–6 months, particularly when there is a known acute cause for CVT, such as minor head trauma, postpartum state, or local infection.

In contrast, prolonged treatment is warranted whenever there is a continuing risk of thrombosis, such as lengthy immobilization, malignant disease, inflammatory disease such as systemic lupus erythematosus or Behcet's disease, inherited thrombophilia or recurrent venous thrombosis[11-12].

In our Study Group Patients:

- All the patients were initially treated with I.V anticoagulants such as i.v heparin or LMWH irrespective of ICH.
- Followed by which patient was started with warfarin with INR maintained between 2 to 3.
- 3 months with patient of transient risk factors and 12 months for recurrent risk factors.

Mortality

- The main cause of death occurring within the first few days of presentation of CVT is Trans tentorial herniation due to a focal lesion, multiple lesions or diffuse oedema.
- While over the next few weeks include trans tentorial herniation, uncontrolled seizures, sepsis, pulmonary embolism, underlying infection or malignancy.
- In our study there were 8 mortality , 1 case was sepsis with CVT,
- 1 case was leukaemia with CVT and 6 patient had a large haemorrhagic transformation on presentation.

DISCUSSION

- CVT is a uncommon form of stroke with a wide variety of clinical presentation with the use of latest neuroimaging methods there is an improvement in early diagnosis which has lead to drastic decrease in morality in current years.
- In our study we have found most of the patients of CVT were in mean age group between 25 to 45 years of age with female predominance .Most of the female patients were in peripartum period with very good prognosis except one patient presented late with involvement of deep sited thrombosis involvement.
- Considering the etiology leading to CVT most common cause was found to pregnancy and pueperium followed by which heavy alcohol consumption and even HIV patient which was less identified in other studies even small number of patient with CVT was found due to other hypercoagulable condition and dehydration secondary to gastroeneteritis. Most common clinical presentation of patients resenting with CVT was headache associated with other clinical features such as focal neurological deficit, blurring of vision, seizures and cranial nerve involvement which was acute to progressive in nature.
- Diagnosis of all the patient of CVT was based on initial CT brain followed by MRV or CT Venography. Most commonly involvement was superior sagittal sinus with combined sinus involvement. And most of the patient on presentation had cerebral infarct on neuroimaging while around 25 % even had hemorrhagic transformation which had poor prognosis as compared to isolated cerebral infarct.
- All the patients were treated with anticoagulants irrespective of intracranial haemorrhage and followed up during the hospital stay in HSK hospital BAGALKOT. There were 8 mortality all of them had a large hemorrhagic transformation with transtentorial herniation while 1 patient had CVT secondary to sepsis with intracranial infection while 1 case had CVT sec AML.

CONCLUSIONS

- CSVT is a multifactorial condition with gender-related specific causes, with a wide clinical presentation, variable aetiologies and prognosis that requires fine medical skills and a high suspicious index.
- Correcting the cause, generally the complications can be prevented.
- Mortality trends have diminished, and with the new technologies, surely it will continue.
- Treatment strategies are aimed at treating the underlying pathology, controlling ICH, and management of seizures or focal deficits caused by cerebral edema or infarction.

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