STUDY OF CEREBRAL VENOUS THROMBOSIS IN MALES

Dissertation Submitted to

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CERTIFICATE

This is to certify that the dissertation entitled **"STUDY OF CEREBRAL VENOUS THROMBOSIS IN MALES**" is the bonafide original work of **Dr. K. ARUNADEVI** in partial fulfillment of the requirements for **D.M (NEUROLOGY) BRANCH – I** Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in August 2013. The period of study was from April 2012 to January 2013.

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DECLARATION

I, **Dr.K.ARUNADEVI,** solemnly declare that the dissertation titled, "STUDY OF CEREBRAL VENOUS THROMBOSIS IN MALES" is a bonafide work done by me at Govt. Stanley Medical College & Hospital during 2010-2013 under the guidance and supervision of **Dr. S.GOBINATHAN, M.D., D.M,** Professor and Head, Department of Neurology Stanley Medical College, Chennai-600 001.

The dissertation is submitted to Tamilnadu, Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of **D.M Degree (BRANCH – I) in Neurology.**

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CONTENTS

ABBREVIATIONS

CVT	Cerebral Venous Thrombosis
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
SSS	Superior Sagittal Sinus
ISS	Inferior Sagittal Sinus
LS	Lateral Sinus
TS	Transverse Sinus
SPS	Superior Petrosal Sinus
IPS	Inferiour Petrosal Sinus
CVP	clival venous plexus
DMCV	Deep middle cerebral vein
BVR	Basal Vein of Rosenthal
ICV	Internal Cerebral Veins
APLA	Anti Phospho Lipid Antibody
ISCVT	International Study for Cerebral Venous Thrombosis
MTHFR	Methyl Tetrahydrofalate Reductase gene
FLAIR	Fluid-Attenuated Inversion Recovery
DWI	Diffusion-Weighted Images
ADC	Apparent Diffusion Coefficient
MRV	Magnetic Resonance Venogram

LMWH	Low Molecular Weight Heparin
ANA	Anti Nuclear Antibody
LAC	Lupus Anti Coagulant
ACA	Anti Cardiolipin Antibody
SAH	Sub Arachnoid Hemorrhage
HE	Haemmorrhage
DEEP	Deep CVT
TOF	Time of flight
CTV	CT Venogram
CECT	Contrast enhanced CT
NECT	Non contrast enhanced CT
T1WI	TI Weighted imaging
FLAIR	Fluid attenuated inversion recovery sequences
ACLA	ANTICARDIOLIPIN ANTIBODY

Introduction

INTRODUCTION

Cerebral venous thrombosis (CVT), is the thrombosis of the intracranial veins or dural sinuses.[1] It is a relatively rare disorder, affecting about 5 persons per million per year with huge regional variations.[2] It accounts less than 1% of all strokes. It has differential geographic distribution with a higher incidence in the Asian countries. In contrast to arterial stroke, thrombosis of the cerebral venous sinuses and the cerebral cortical veins most often affects children and young adults.

Its presentation is highly variable, etiological factors are diverse and more heterogeneous making cerebral cortical venous thrombosis (CVT) a distinctively unique entity.

The Virchow's triad, which compromises the features of endothelial damage, stasis and hypercoagulability of blood, plays a very important role in the pathogenesis of cerebral venous sinus thrombosis. These haemodynamic factors vary with each patient. They may operate together incidentally or accidentally to produce the clinical manifestation of cerebral cortical venous sinus thrombosis.

Before the availability of computed tomography (CT) and magnetic resonance imaging (MRI), CVT was considered to be a disorder of infectious etiology that usually results in bilateral or alternating focal neurological deficits, which was associated with seizures and coma and usually leading to death. In fact, CVT was usually diagnosed at autopsy or sometimes at angiography, i.e., in patients with severe clinical manifestations. The widespread availability of CT- and MRI-scans has totally changed our knowledge about the disease and on its wide clinical spectrum.

Nowadays, in western countries CVT is regarded as a disorder of non-infective origin with varied clinical presentations with a favourable outcome and a case-fatality rate of less than 10%.[1] Heparin is the treatment of choice and the prognosis nowadays is usually good.

CVT has been a disease associated with a considerable morbidity in the general population, more so in females during their post partum period and with a history of intake of OCP. But recent studies show an increasing incidence in males also. This study aims to try to evaluate risk and etiological factors that possibly play an important role in the causation of CVT in males in this part of the city.

Aim of the Study

AIM OF THE STUDY

To study the risk and etiological factors in pathogenesis of Cerebral Venous Thrombosis and the varied clinical presentation in males.

Review of Literature

REVIEW OF LITERATURE - I

ANATOMY OF CEREBRAL VENOUS SYSTEM

The venous system of the brain is distinct from the systemic ones. They lack valves and may have bidirectional flow. The dural venous sinuses and cerebral veins do not travel with their arterial counterparts and hence their drainage territories do not mirror arterial distributions. Therefore, a venous "stroke" looks and behaves differently from an arterial occlusion. Connections exists between venous sinuses and the veins of scalp, face and neck. They not only provide alternate route, but also serve as a path by which infection can spread to venous sinuses from these areas to cause cerebral venous sinus thrombosis.

Cerebral venous system can be divided into a superficial and a deep system. The superficial system includes the sagittal sinus and the draining cortical veins that drain the superficial surfaces of both the cerebral hemispheres. The deep system comprises of lateral sinus, straight sinus and sigmoid sinus along with the draining deeper cortical veins . Both these systems mostly drain into internal jugular veins.

Cerebral Veins are divisible into external and internal veins which drain the external surface and the internal region of the cerebral hemispheres respectively. The external cerebral veins drain the superficial part of cerebral hemispheres. The superior cerebral veins drain the supero lateral and the medial surface of the cerebral hemisphere. They ascend upwards, pierce the arachnoid mater, traverse the subdural space and drain into the superior sagittal sinus. The middle cerebral veins drain into the cavernous sinuses and the inferior cerebral veins into lateral sinuses.

The internal cerebral veins drain blood from the deeper part of cerebral hemispheres into the great cerebral vein of Galen. The basal veins of Rosenthal drain part of lower frontal lobe and insula and are joined by inferior striatal veins and terminate either in the internal cerebral veins or directly into great cerebral vein. The two internal cerebral veins drain mainly the basal ganglia, thalamus and hypothalamus to unite to form the great cerebral vein, which joins the inferior sagittal sinus to form the straight sinus. Connections exist between external and internal venous system, which allows blood to take alternative route, if needed.

SUPERIOR SAGITTAL SINUS

It is situated in the attached margin of falx cerebri. It commences at crystal galli and end posteriorly into one of the (usually the right) transverse sinus. They are occupied by arachnoid granulations for CSF absorption.

INFERIOR SAGITTAL SINUS

It is situated in the free margin of falx cerebri. It passes posteriorly and drains into the straight sinus.

STRAIGHT SINUS

It is situated at the junction of falx cerebri and tentorium. It runs posteriorly and drains into the transverse sinus in the side opposite to which the superior sagittal sinus has drained. It is formed by the union of great cerebral vein of Galen and inferior sagittal sinus.

TRANSVERSE SINUSES

These begin at internal occipital protuberances to lie in the attached margin of tentorium and pass anteromedially to continue as sigmoid sinuses. The right transverse sinus is usually bigger than the left

one. In about 4% cases the left sinus may be absent or hypoplastic . The superior sagittal sinus and straight sinuses drain into one of the transverse sinus, usually the right.

SIGMOID SINUS

They continue anteriorly over the mastoid part of temporal bone to continue as internal jugular vein at jugular foramen.

CAVERNOUS SINUSES

They lie one on each side of the sphenoid bone. They receive blood from ophthalmic veins, several of the anterior inferior cerebral veins, the sphenoparietal sinus and the pituitary vein. They are traversed by number of structures, involvement of which causes clinical manifestation of cavernous sinus thrombosis. The Internal carotid artery wrapped by sympathetic plexus passes through it while abducent nerve lies inferolaterally. The oculomotor and trochlear nerves and the first and second divisions of the trigeminal nerve lie in the lateral wall of the sinus. The two sinuses are connected by the valveless circular sinus

SUPERIOR AND INFERIOR PETROSAL SINUSES

The superior petrosal sinus (SPS) courses posterolaterally along the top of the petrous temporal bone, extending from the cavernous sinus to the sigmoid sinus. The inferior petrosal sinus (IPS) courses just above the petrooccipital fissure from the inferior aspect of the clival venous plexus to the jugular bulb.

SPHENOPARIETAL SINUS

The sphenoparietal sinus (SPS) courses around the lesser sphenoid wing at the rim of the middle cranial fossa. The SPS receives superficial veins from the anterior temporal lobe and drains into the cavernous or inferior petrosal sinus.

CLIVAL VENOUS PLEXUS

The clival venous plexus (CVP) is a network of interconnected venous channels that extends along the clivus from the dorsum sellae superiorly to the foramen magnum. The CVP connects the cavernous and petrosal sinuses with each other and with the suboccipital veins around the foramen magnum.

Figure 1: Cerebral venous sinuses - Anatomy

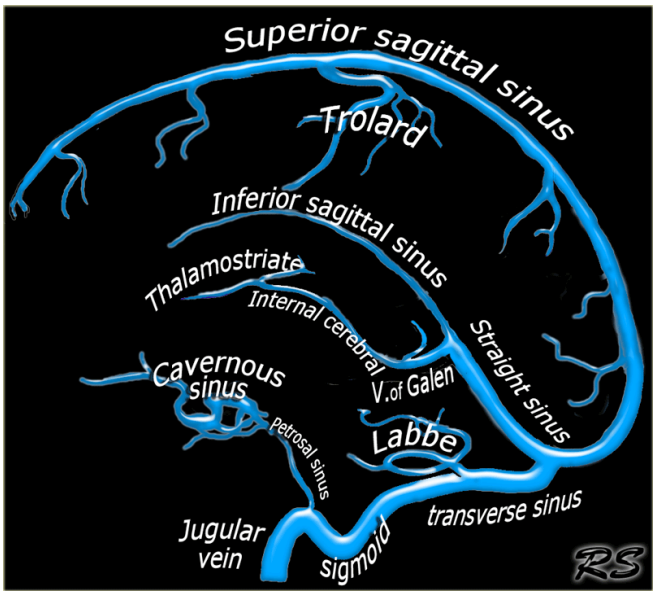


Figure 2: Anatomy of cerebral venous sinuses

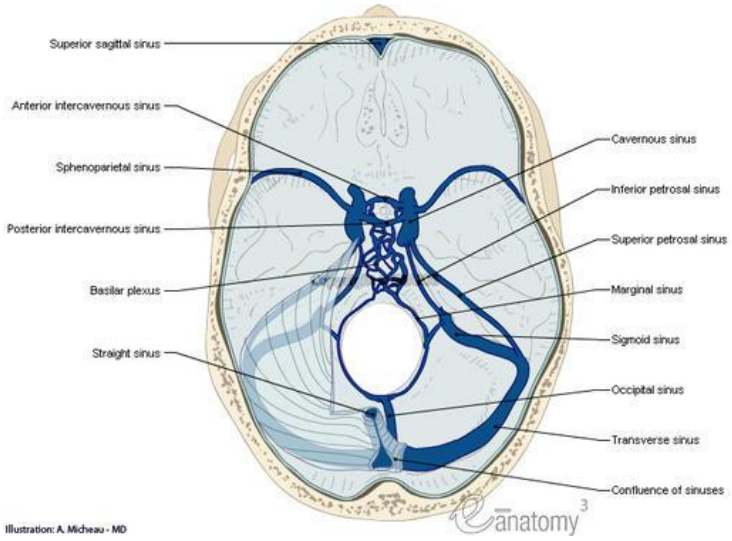


Figure 3: Anatomy of Cavernous sinus

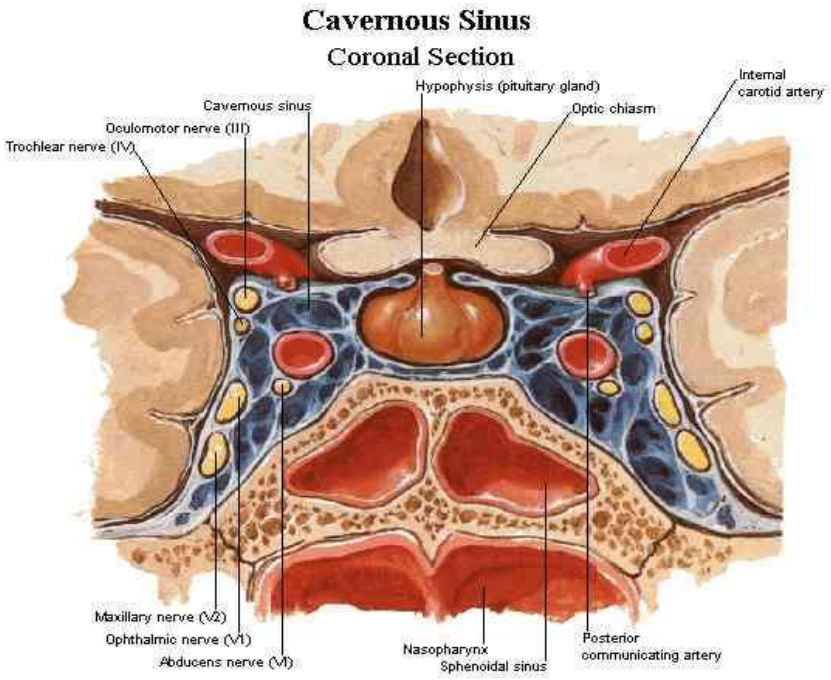
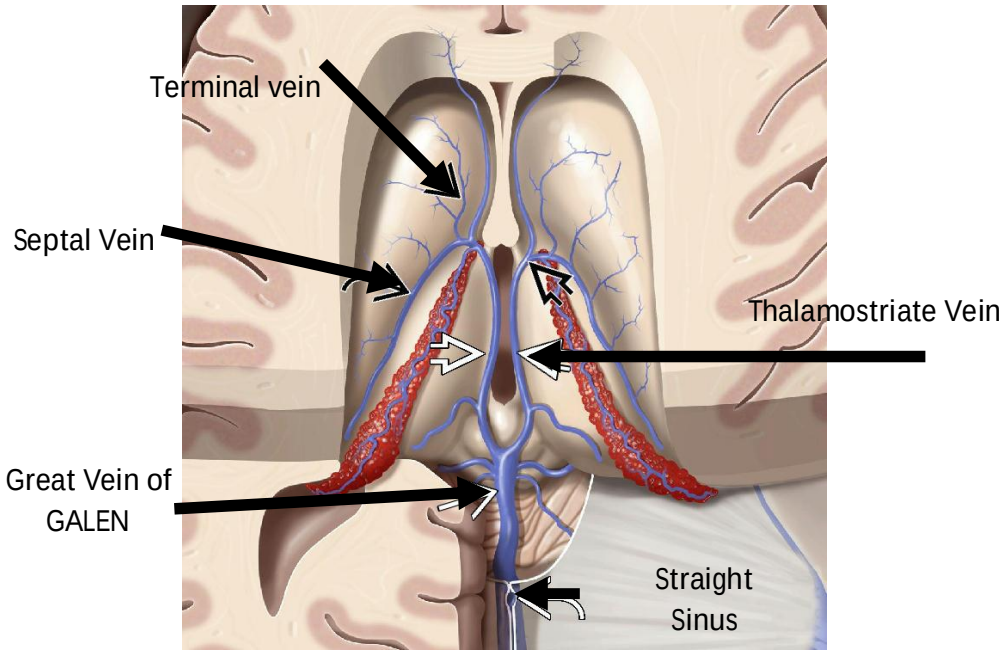


Figure 4: Anatomy of Deep Venous System



CEREBRAL VEINS

The cerebral veins are subdivided into three groups:

(1)Superficial ("cortical" or "external") veins

(2) Deep cerebral("internal") veins

(3) Brainstem/posterior fossa veins.

(1) SUPERFICIAL CORTICAL VEINS

The superficial cortical veins consist of a superior group, a middle group, and an inferior group. Between 8-12 unnamed superficial veins course over the upper surfaces of the cerebral hemispheres, generally following convexity sulci. They cross the subarachnoid space and pierce the arachnoid and inner dura before draining into the SSS. In many cases, a dominant superior cortical vein, the **vein of Trolard**, courses upward from the sylvian fissure to join the SSS.

MIDDLE CORTICAL VEINS.

The most prominent vein in this group is the **superficial middle cerebral vein**(SMCV). The SMCV begins over the sylvian fissure and collects numerous small tributaries from the temporal, frontal, and parietal opercula that overhang the lateral cerebral fissure.

INFERIOR CORTICAL VEINS.

These veins drain most of the inferior frontal lobes and temporal poles The deep middle cerebral veins (DMCV) collects tributaries from the insula, basal ganglia and anastomoses with the basal vein of Rosenthal (BVR). The BVR courses postero superiorly in the ambient cistern, curving around the midbrain to drain into the great vein of Galen.

DEEP CEREBRAL VEINS

The deep cerebral veins may also be subdivided into three groups: (A) medullary veins, (B) subependymal veins, and (C) deep paramedian veins.

MEDULLARY VEINS.

Innumerable small, unnamed veins originate between 1-2 cm below the cortex and course straight through the white matter towards the ventricles where they terminate in the subependymal veins. These veins are generally in apparent on imaging studies throughout most of their course until they converge near the ventricles.

(B) SUBEPENDYMAL VEINS.

The subependymal veins course under the ventricular ependyma, collecting blood from the basal ganglia and deep white matter (via the medullary veins). The two most important ones are the septal veins and the thalamo striate veins. The **septal veins** curve round the frontal horns of the lateral ventricles, then course posteriorly along the septum pellucidum. **The thalamostriate veins** receive tributaries from the caudate nuclei and thalami, curving medially to unite with the septal veins near the foramen of Monro to form the two internal cerebral veins.

(A) DEEP PARAMEDIAN VEINS.

Two important paramedian veins, the **internal cerebral veins** (ICVs) and **vein of Galen** (V of G) provides drainage for most of the deepbrain structures.

The ICVs are paired paramedian veins that course posteriorly in the cavum velum interpositum, the thin invagination of subarachnoid space that lies between the third ventricle and the fornices. The ICVs terminate in the rostral quadrigeminal cistern by uniting with each other and the basal vein of Rosenthal to form the vein of Galen.

The **vein of Galen (great cerebral vein)** curves posterosuperiorly under the splenium of the corpus callosum, uniting Brainstem/Posterior Fossa Veins. The veins that drain the midbrain and posterior fossa structures are likewise divided into three groups: (1) a superior ("galenic") group, (2) an anterior (petrosal) group, and (3) a posterior group.

(i) SUPERIOR (GALENIC) GROUP.

As the name implies, these veins drain superiorly into the vein of Galen. Major named veins in this group are the precentral cerebellar vein, the superior vermian vein, and the anterior pontomesencephalic vein. The precentral cerebellar vein (PCV) is a single midline vein that lies between the lingula and the central lobule of the vermis. It terminates behind the inferior colliculi by draining into the V of G. The superior vermian vein runs over the top of the vermis, joining the PCV and draining into the great vein of Galen . The APMV covers the cerebral peduncles.

(ii) ANTERIOR (PETROSAL) GROUP.

The petrosal vein (PV) is a large venous trunk that lies in the Cerebello pontine angle cistern, collecting numerous tributaries from

the cerebellum, pons, and medulla. The PV and its tributaries form a prominent star-shaped vascular collection that is sometimes termed the "petrosal star" on AP digital substraction angiography or coronal CT venogram.

(iii) POSTERIOR (TENTORIAL) GROUP.

The most prominent veins in these groups are the inferior vermian veins which are paired paramedian structures that curve under the vermis and drain the inferior surface of the cerebellum.

ETIOLOGY

Causes and Risk factors for Cerebral Vein thrombosis:[3]

COMMON

- Oral contraceptives
- Prothrombotic conditions
- Deficiency of proteins C, S, or antithrombin III
- Resistance to activated protein C/V Leiden
- Prothrombin gene mutations
- Antiphospholipid, anticardiolipin antibodies
- Hyperhomocysteinemia
- Puerperium, pregnancy
- Metabolic (dehydration, thyrotoxicosis, etc.)

Less Common

- Infection
- Mastoiditis, sinusitis
- Meningitis
- Trauma
- Neoplasm-related

Rare but Important

- Collagen-vascular disorders (e.g., APLA syndrome)
- Hematologic disorders (e.g., polycythemia, Thrombocythemia, Leukemia)
- Inflammatory bowel disease
- Vasculitis (e.g., Behçet)
- Drugs (Oral contraceptives, Asparaginase)
- Neurosurgical procedures, Lumbar puncture

Many conditions can cause or predispose to cerebral venous sinus thrombosis . They include medical, surgical and obstetrical causes . Conditions that predispose to cererbral venous sinus thrombosis include genetic and acquired prothrombotic disorders, haematological conditions, inflammatory systemic disorders, cancer related prothrombotic states, pregnancy and puerperium, infections , local causes such as tumours, arteriovenous malformations, trauma, central

nervous system infections and infections of the ear, sinus, mouth, face and neck.[1] Diagnostic and therapeutic procedures such as, lumbar puncture, jugular venous catheterisation and drugs such as hormonal contraceptives, hormone replacement therapy, steroids when especially combined with a lumbar puncture predispose to cerebral venous sinus thrombosis.

Genetic hypercoagulable conditions:

In the International Study for Cerebral Venous Thrombosis (ISCVT)[1], 44% of the patientswere found to have more than one cause or predisposing factor. Congenital or genetic thrombophilia are a group of diseases which cause a majority of prothrombotic states according to the same study.[1] Antithrombin III deficiency, protein C and protein S deficiency , factor V Leiden or the prothrombin gene mutations,[4,5] elevated factor VIII levels[6] and elevated levels of von Willebrand factor are associated with an increased risk of CVT.[6] The protein C promoter CG haplotype gene polymorphisms in the coagulation and fibrinolytic systems, bears no independent association in the causation of CVT. However, this polymorphism increases the risk in the carriers of the factor II G20210A mutation with an odds ratio rising from 14.7 (95% CI: 2.83-75.3) with the factor II mutation alone to 19.8 (95% CI: 2.1-

186.5) in the combination of both the mutations.[7] For classic congenital thrombophilia and hyperhomocysteinaemia,[8] the risk is increased when the protein C promoter CG haplotype is associated with estrogen treatment [7] The testing for congenital thrombophilia should be systematically performed in patients with CVT, even when there a clear cause has been found, for the following important reasons: (i) the presence of congenital thrombophilia potentiates the risk of CVT and (ii) it is important to look for the disorder in family members to start them on preventive measures. [4, 5]

A study from France demonstrated that factor VIII elevations were commonly associated with cerebral venous thrombosis[6, 11]

The specific thrombophilias involved in cerebral venous thrombosis may differ with respect to disorders associated with deep venous thrombosis.[12].

Hyperhomocysteinaemia:

It is an independent and strong risk factor for CVT, which is present in 27-43% of patients and in 8-10% in the community. [8, 13, 14] The post-methionine load increment of homocysteine has been found to be strongly associated with CVT [8] but not confirmed. [13] No

independent association has been found between the C677T mutation in the methylene tetrahydrofolate reductase gene (*MTHFR*) and CVT. [8, 13]

Acquired hypercoagulable disorders:

Acquired coagulation disorders that are recognized as a cause or predisposing condition for cerebral venous thrombosis include disseminated intravascular coagulation, heparin-induced thrombocytopenia [15], plasminogen deficiency, epsilon aminocaproic acid treatment, sickle cell disease, polycythemia vera, paroxysmal nocturnal hemoglobinuria, thrombocythemia, antiphospholipid antibody syndrome[16], nephrotic syndrome, thyrotoxicosis,[17,18,19] and hypercoagulability associated with malignancy. Anemia due to iron deficiency and other causes has also been associated with cerebral venous thrombosis.[20,21,22,23,24]

Inflammatory disorders:

Conditions such as lupus erythematosus, Behçet disease, sarcoidosis, ulcerative colitis, Crohn disease, and Wegener granulomatosis are associated with cerebral venous thrombosis.[25,26,27,28,29,30] Cerebral venous thrombosis may be the first manifestation of an inflammatory systemic disease.

Structural damage to venous sinuses:

Head trauma and intracranial surgeries are among the most common structural etiologies of cerebral venous thrombosis. Cutaneous infections or contusions can injure the diploic veins that connect to the scalp via emissary veins and drain in the superior sagittal sinus.

Miscellaneous causes:

Other causes of cerebral venous sinus thrombosis reported in various studies are spontaneous intracranial hypotension,[31] thalidomide,[32] Cushing's syndrome,[33] tamoxifen,[34] erythropoietin,[35] high altitude,[36] phytoestrogens[37] and even Shiatsu massage of the neck.[38]

Arteriovenous malformations, tumors, carcinomatous meningitis, arachnoid cysts, local or surgical trauma to the jugular vein, high altitude exposure,[39] and electrical injury have also been associated with cerebral venous thrombosis.[40] Intracranial hypotension and low CSF pressure syndromes have been associated with cerebral venous thrombosis.[41,42,43,44,45] Thrombosis has also recently been noted as a complication of ventriculoperitoneal shunting.[46].

Idiopathic causes:

In 20% to 35%. of cases the etiology of cerebral venous sinus thrombosis remain unknown. [47]

Mechanisms Leading to the Clinical Manifestations

Two different mechanisms have been postulated and identified; however, they are interrelated in many cases. [3]

The occlusion of a main sinus or the feeding cortical veins leads to vascular congestion ,which results in localized brain oedema and resultant venous infarction . A block in the major sinus leads to intracranial hypertension whereas a block in deep cortical veins leads to oedema, venous infarcton and petechial haemorrhages that merge with each other and form large haematomas. Cytotoxic oedema caused by local ischemia, subsequently damages the energy dependent cellular membrane pumps and induce intracellular swelling. [3] Vasogenic oedema developing due to disruption of the blood brain barrier and engorgement of the brain interstitium with blood eventually leads to neuronal swelling.

The occlusion of a major sinus results in intracranial hypertension due to impaired absorption of cerebrospinal fluid by the arachanoid villi. The ventricles do not dilate and hydrocephalus does not develop as ventricular communication with the subarachanoid space remains patent.

Pathology

When thrombus forms in a dural sinus, venous outflow is restricted. This results in venous congestion, elevated venous pressure, and hydrostatic displacement of fluid from capillaries into the extracellular spaces of the brain. The result is blood-brain barrier breakdown with vasogenic edema. If a frank venous infarct develops, cytotoxic edema ensues.

CLINICAL MANIFESTATIONS

Cerebral venous thrombosis presents with a wide spectrum of clinical manifestations and modes of onset that mimics many other neurological disorders which leads to frequent misdiagnoses or delay in diagnosis.

HEADACHE

Headache is the most frequent symptom in cerebral venous sinus thrombosis. The two plausible hypothesis that have been proposed for the mechanism of headaches include the stretching of nerve fibres in the walls of the occluded sinus and local inflammation caused by it as suggested by the enhancement of the contrast in the walls of sinus surrounding the clot. [2]

Headache is a consistent complaint in patients from whom a reliable medical history could be obtained . [48] Most patients who present with other neurological symptoms often complain of headache at admission or report a history of headache of unusual type that started a few days or weeks earlier.[48]

Headache may occur due to intracranial hypertension. Patients with a prolonged course or with delayed clinical presentation may have papilloedema. [49]

Headache may be the only manifestation in CVT , though it may be difficult to differentiate from other causes like intracranial hypertension, subarachnoid hemorrhage or meningitis.[10,50] Isolated headache may be of the thunderclap type, mimicking a subarachnoid

hemorrhage.[10] .Isolated headaches are usually associated with lateral sinus thrombosis.[2] Since headache is almost always the first symptom of CVT, it is important to have a high index of suspicion to diagnose this treatable entity.

Isolated focal neurological deficits

In cerebral venous sinus thrombosis the presentation may be a transient focal neurological deficit mimicking a transient ischemic attack or may be a long-lasting focal neurological deficits due to stroke either due tovenous ischemia ,intra-cerebral haemorrhage or edema;

The diagnosis is sometimes easily made in a patient with acute onset headache who has a known predisposing condition, such as puerperium. Sometimes the diagnosis will be picked up during imaging taken for a suspected arterial stroke.

Diffuse encephalopathy with seizures

Patients with parenchymal lesions, may present with a more severe clinical scenario which may include various degrees of coma, motor deficits or aphasia and seizures (focal or generalized seizures, including status epilepticus). Seizures may be the presenting features in

patients with parenchymal lesions, with sagittal sinus and cortical vein thrombosis. [51]

Other clinical presentations

Varied clinical presentations have been described in cerebral venous sinus thrombosis [1,52,53,54] which includes attacks mimicking migraine with aura, isolated psychiatric disturbances, pulsatile tinnitus, isolated or multiple cranial nerve involvement or subarachnoid hemorrhage .

Clinical manifestations based on site of venous occlusion

Different types of clinical manifestations occur with involvement of the different sinuses :

In occlusions of superficial cortical veins ,sensory or motor deficits, seizures may be the presenting features.

In superior sagittal sinus thrombosis motor deficits that are sometimes alternating or bilateral may be present . Seizures are also commonly associated. Features of intracranial hypertension can also be the presenting manifestation in SSS thrombosis.

Thrombosis of the lateral sinus may present as an isolated intracranial hypertension. Patients may also have associated aphasia when the left transverse sinus is involved.

Thrombosis of deep cerebral veins leads to a severe clinical presentation with coma, delirium and bilateral motor deficits, but symptoms may be of milder intensity when the thrombosis is limited. [55]

In cavernous sinus thrombosis, usually presents with orbital pain, chemosis, proptosis and oculomotor palsies.

Imaging in cerebral venous thrombosis

The key to the diagnosis of CVT is the documentation of the occluded vessel or of the intravascular thrombus. The gold standard is the combination of MRI, which visualizes the thrombus , with magnetic resonance venography (MRV), which shows the nonvisualization of the vessel. [4, 56]

Cortical venous thrombosis with or without sinus involvement

Computed Tomography

CT scan of Brain with contrast and coronal reconstruction shows the following:[74]

Bony abnormalities, PN sinuses and mastoid Dense triangle sign-dural sinuses or deep vein can shown as hyperdense, round or triangular structures on non-contrast axial cuts indicating presence of thrombus within.

Cord sign-Cerebral cortical vein is seen as high density, thin, linear structure. This is a rare but a specific sign.

Empty delta sign; This seen in contrast CT in SSS on coronal view. The contrast enhances the walls but middle lumen with thrombus does not enhance.

Deep venous system occlusion manifests as infarct, oedema and haemorrhages in the thalamus and basal ganglia.

CT VENOGRAM

Depicts thrombus as filling defect in cortical veins

Abnormal collateral channels (e.g., enlarged medullary veins) are seen

Limited role in chronic CVT (organizing thrombosis also enhances).

MRI

TlWI: In T1 sequence, the clot is hyperintense in the acute phase. Venous infarct in T1 is characterised by gyral swelling, associated with hypointense edema, and may be associated with hemorrhage

T2WI : The clot is often hypointense mimicking flow void which later becomes hyperintense Venous infarct in T2 shows gyral swelling, hyperintense edema, and may be .hemorrhagic.

FLAIR : In FLAIR sequence the thrombus usually hyperintense, oedema looks hyperintense.

T2 GRE : Clot will be hypointense with blooming

DWI : DWI/ ADC imaging findings heterogeneous depending on the presence of ischemia, type of edema, hemorrhage

T1 CONTRAST

In the acute/early subacute state the clot enhances in the periphery

MRV

2D time of flight (TOF) MRV depicts thrombus as sinus discontinuity, loss of vascular flow signal .

CONTRAST ENHANCED MRV (CE-MRV)

• Depicts non enhancing thrombus &small veins than TOF

MR PERFUSION

T2 Gadolinium perfusion may show extensive venous congestion, but without perfusion deficits . It may play a role in detecting venous congestion vs venous infarction in CVT

Ultrasonographic Findings

• Transcranial Doppler (TCD) ultrasound

Monitor venous flow velocities at ICU bedside

Angiographic Findings

Conventional: More accurate than MRI, particularly for isolated cortical vein thrombosis

Imaging Recommendations

NECT, CECT scans +/- CTV

Conventional DSA most sensitive for CVT (useful if intervention is planned).

Interventional

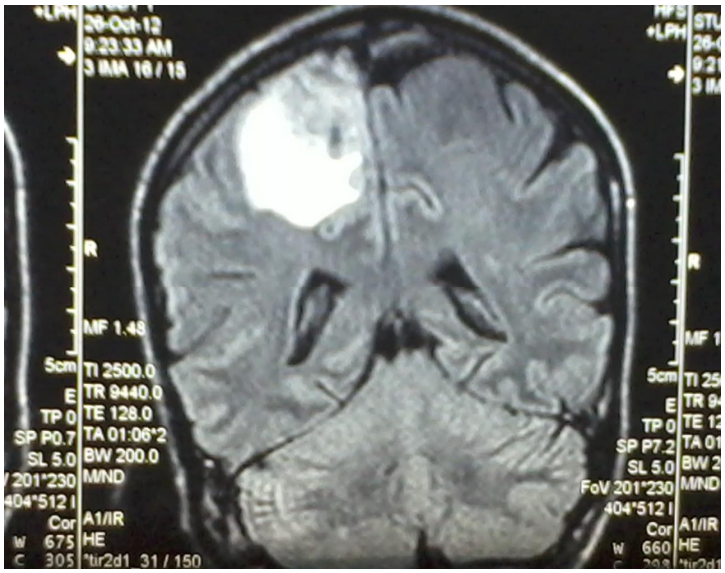
Treatment with thrombolytics and/or mechanical de clotting.

In the acute stage of thrombosis, MRI may show flow artefacts that can lead to false positives and the lack of hyperintense signal on T1- and T2-weighted images. [2]

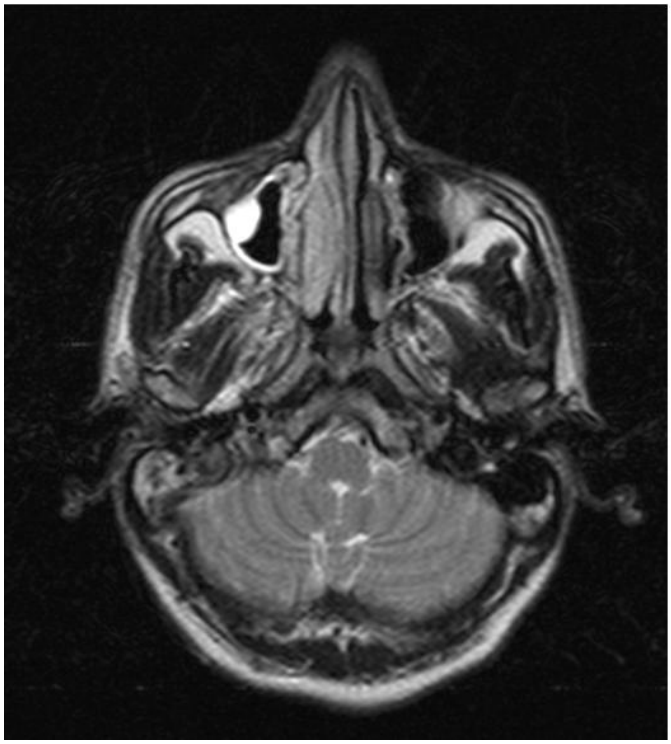
During the first 2 to 5 days, the thrombosed sinus appears as an isointense signal on T1-weighted sequences and a hypointense signal on T2-weighted sequences[2] The diagnostic yield of MRV alone, is limited because it does not make a clear differentiation between an occluded sinus and hypoplasia, particularly for lateral sinuses. [4, 56] Even with the combination of MRI and MRV, the diagnosis can still be difficult, in the setting of isolated cortical vein thrombosis . If the characteristic cord sign is not present on non-contrast enhanced CT or MRI-scan, [57, 58] a conventional angiography may sometimes be required. [59] The inter observer agreement for the diagnosis of the location of CVT is not perfect, particularly in the case of cortical vein thrombosis. [60]

Several studies have shown the value of T2-weighted sequences: in contrast to T1 , in T2, the thrombus exhibits a hypointense signal with the magnetic susceptibility effect, the signal being similar to that of

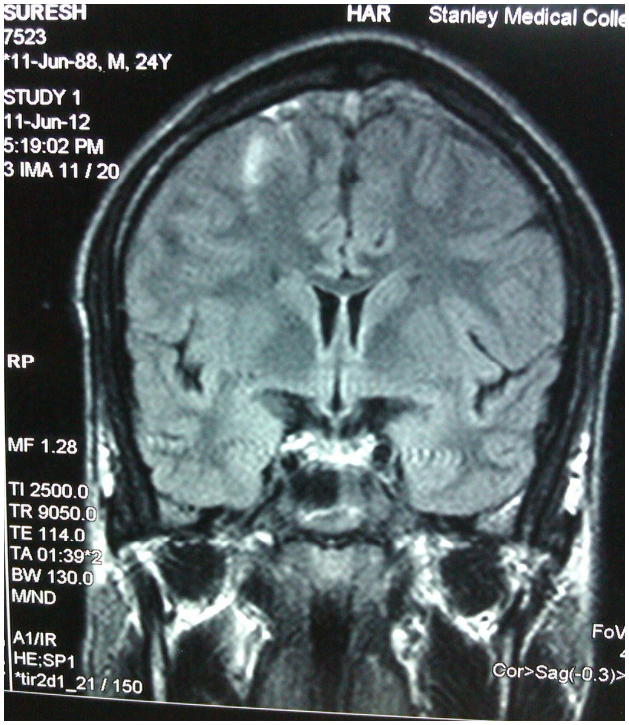
T-2 FLAIR – SEQ : SHOWING HAEMORRHAGE



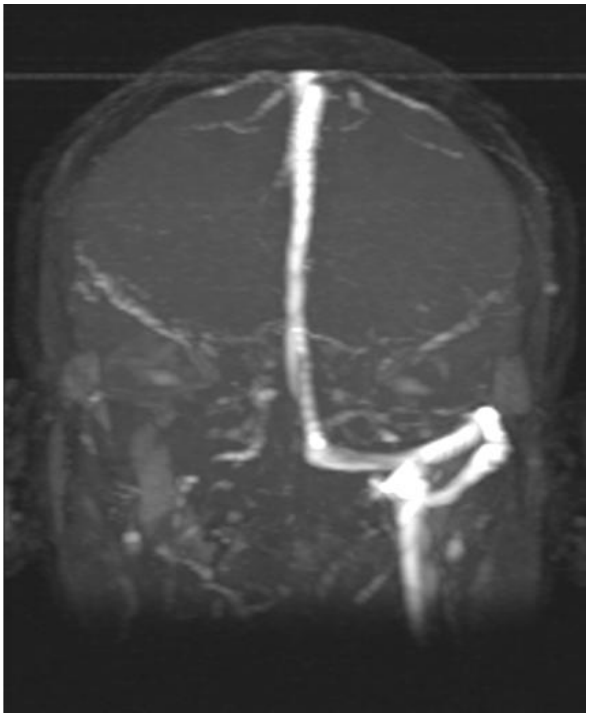
T-2 AXIAL SHOWING MASTOIDITIS WITH TRANSVERSE SINUS THROMBOSIS



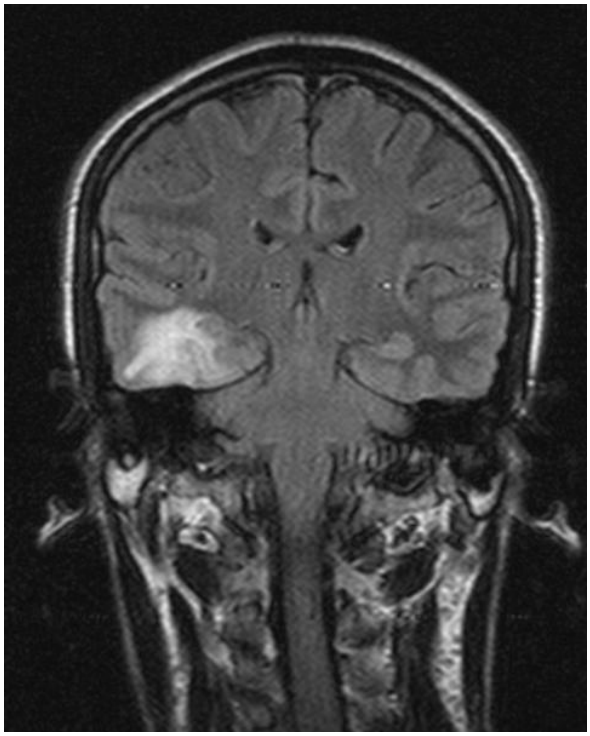
T2 – FLAIR SHOWING SAH WITH SUPERIOR SAGITAL SINUS THROMOBSIS



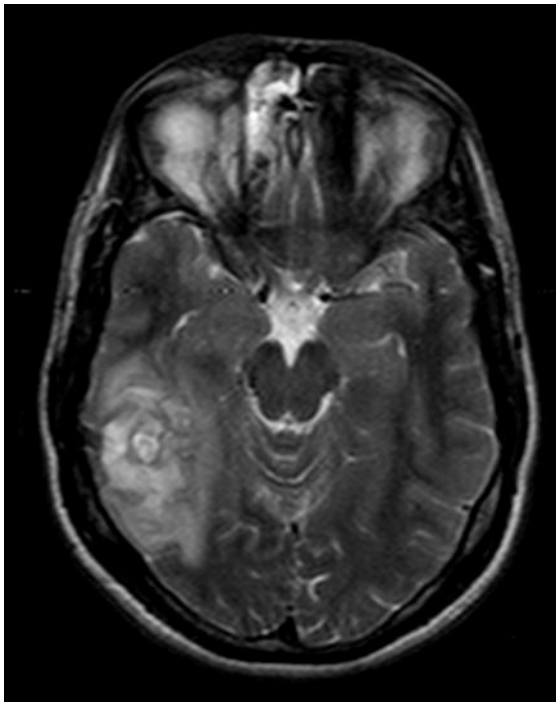
MR VENOGRAM SHOWING RT. TRANSVERSE SINUS THOMBOSIS



T2 – FLAIR SHOWING EDEMA IN RIGHT TEMPORAL LOBE



T2 AXIAL SHOWING HAEMORRHAGE INFARCT IN THE RIGHT PARIETAL LOBE



an intracerebral hemorrhage.[61,62,63] A hypointense signal on T2-images is present in 90% of sites of CVT on the first MRI-scan, while a hyperintense signal is detected on T1-images.[63] This excellent sensitivity of T2 sequences is of major interest within the first 3 days when thesensitivity of T2 sequences is higher than 90% and that of T1 -sequences in only 70%.[2,63] Accordingly, a thrombus located in cortical veins, even in the absence of visible occlusion on MRV, is more easily detected with T2 (97%) than with T1 (78%) or fluid-attenuated inversion recovery (FLAIR) <40%).[63] The presence of a hyperintense signal of the thrombosed sinus on diffusion-weighted imaging may be useful to predict nonrecanalization.[66]

Although none of the MRI sequences (T1, T2, FLAIR) has a sensitivity and specificity of 100%, the diagnostic yield of their combination together with MRV is so high that conventional angiography is nowadays almost not required in patients who can undergo MRI.[2]

Neuroimaging of parenchymal abnormalities with MRI and DWI

In contrast to arterial strokes, brain imaging is less significant in the diagnosis of CVT.[2] It usually shows only nonspecific lesions, such

as intracerebral hemorrhages or infarcts, oedema associated with infarcts or hemorrhages. It can also be normal in up to 30% of patients. [2]

The most common pattern is a heterointense signal with normal or increased apparent diffusion coefficient (ADC), corresponding to vasogenic edema. [64,65,70,71,73] Only one study showed a decreased ADC in most patients, suggesting a cytotoxic edema. [72] Rarely there may be a pattern of decreased diffusion with complete resolution of the lesion on follow-up in T2-weighted imaging, mostly in patients with seizures. [73]

D-dimer measurement

Several studies [75,76,77,78,79] have tested the importance of D-dimer measurements, because in patients with deep vein thrombosis of the legs, a value below 500 ng/mL has a high negative predictive value., In patients with recent CVT, there is an increase in D-dimer concentrations; this implies that a low value of D-dimer makes the diagnosis of CVT unlikely. [76,77,78] However, the negative predictive value of low D-dimer concentrations is good in patients with encephalic signs, who anyway should undergo MRI, but not in those with isolated headache. [79]

Lab Studies.

After making a diagnosis of CVT, lab investigations are necessary to look for the various contributory causes for the prothrombotic state. Investigations include complete blood count to exlude anaemia ,polycythemia and megalo blastic states .Abnormally high ESR might favour a collagen vascular disorder. ANA and Anti-Ds DNA are to be done in suspected collagen vascular disorder. Antiphospholipid and anticardiolipin antibodies are done when primary or secondary APLA syndrome is suspected. Elevated SGPT and serum protein is helpful in screening for liver disease. Decreased albumin: globulin ratio, with hyper gammaglobulinemia favours a hyper viscosity state. Sickle cell preparation or hemoglobin electrophoresis may be required in relevant cases. Urine protein is done to screen for nephrotic syndrome. D-dimer values may be beneficial in screening patients for venous thrombosis. Evaluation for protein S, C, antithrombin III, lupus anticoagulant, and factor V Leiden mutation should not be made while the patient is on anticoagulant therapy, Lumbar puncture is to be done if a meningitic process is suspected to be the cause for the CVT. EEG may be helpful in evaluating a seizure focus, may be normal, may show mild generalized slowing, or show

focal abnormalities if a unilateral infarct occurs, but it does not genuinely influence diagnosis and management.

The Diagnostic steps should include the following.

(1) To recognize CVT a high index of suspicion and good clinical skill is needed,

(2) Rule out other possible diagnosis by supporting investigations like CT and MRI, or sometimes only MR/MR venogram helps to rule out CVT.

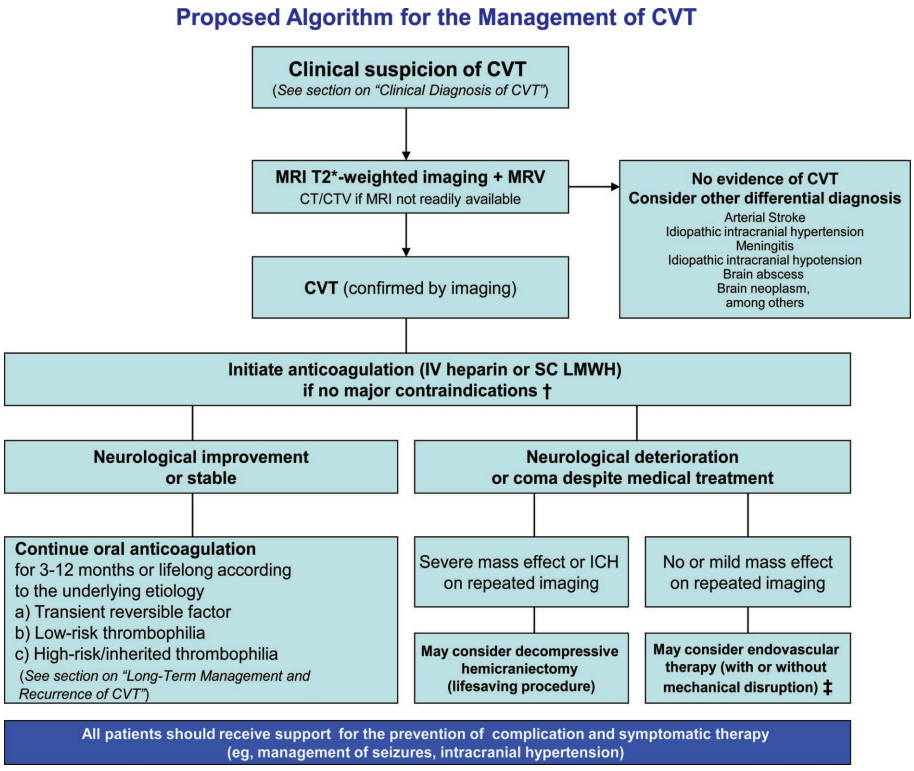
(3) Clinical evaluation to assess risk factors of thrombophilia by history and physical examination and lab tests even when they is not confirmed thrombus in any of the venous sinuses.

(4) Identify all the possible acquired causes investigate when necessary, if CVT is the cause or strong possibility.

(5) Look for possible hereditary causes—if identified or strongly suspected consider prolonged anticoagulation and avoidance of all acquired risk factors for thrombosis.

TREATMENT

Current treatment option for CVT include antithrombotic therapy with un-fractionated heparin, Low Molecular Weight Heparins, Oral anticoagulants, intravenous thrombolytic therapy, local thrombolysis by selective sinus catheterization and combination of thrombolysis and anticoagulation.



Anticoagulation with Heparin is indicated for most cases of venous sinus thrombosis patients with or without haemorrhage into venous infarct, appears to of benefit. Duration of chronic

anticoagulation with warfarin is not standardised and decision should be based on the reversibility of the underlying cause, and anatomic issues of recanalisation and collateral flow. Transvenous cannulation of the affected sinus with catheter directed thrombolysis and mechanical removal of thrombus may be indicated in patients have severe deficits from involvement of deep venous system or extensive involvement of superficial sinuses.

Review of Literature II

REVIEW OF LITERATURE – II

1. In a retrospective analysis of 71cases of CVT by **Vembu P, John JK et al.**[80] treated at Ibn Sina Hospital, Kuwait, showed male to female ratio of 1:1.5and the incidence of Headache was (93%), seizures was (31%), and focal neurological signs was (37%). Papilledema with raised intracranial pressure was seen in 20 patients (28%), ovarian hyper-stimulation syndrome with CVT in one t, Neuro-Behcet`s in 10% (n=7). The venous sinuses involved were superior sagittal sinus in 59% (n=42), and transverse and straight sinuses in 54% (n=38). Hemorrhagic venous infarctions were seen in 18% (n=13).

2. Another study by **Abdulkader Daif et al.**[81] where 40 cases of CVT was analysed, In this study, headache was present in 82%, papilledema in 80%, focal motor deficits in 27%,cranial nerve palsies in 12%, coma in 10%, seizures in 10%, amd meningeal signs in 2%. The etiology included coagulopathies in 27%,bechets in 10%, SLE in7%, tumours in 7%,infections in 7% and unknown cause in 25%.

3. In a retrospective analysis of 49 patients with confirmed CVT[82], 38 were female. Patient's age varied between 16 and 75 years, with an average of 42.6 years. Thrombotic risk factors were found in 43 patients; the most frequent was dyslipidemia (n = 22) followed by oral contraceptive use (18). Right transverse sinus was the most common location of thrombosis (36). Only in four cases thrombosis did not involve the lateral sinuses.

4. **Algahtani HA et al.[83]** retrospectively analysed 111 CVT patients from January 1990 – November. 92 were adults and 19 were children. Among adults, females predominated, while more boys were affected than girls. The mean age of presentation was 29.5 years. The most common clinical presentations were headache, focal neurologic deficits, seizures, papilledema, and decreased level of consciousness. The main risk factors identified were pregnancy/ puerperium, antiphospholipid antibody syndrome, oral contraceptive pills, malignancy, and infections. Multiple sinuses were affected in 51 patients (45.9%). When a single one was involved, the superior sagittal (24.3%) was the most common. Seventy-four patients recovered completely, 23 patients recovered

partially, and 10 patients died. Bad prognostic factors included incurable co-morbid conditions, late presentation, and status epilepticus.

5. In a prospective study in Sudan, during the period from February 2001-October 2006 by **Mohamed-Nagib A Idris et al.**[84] included 15 patients, where 12 were females and 3were males with a mean age of presentation 0f 33.9. Headache (n=15), papilledema(n=13), paresis (n=3), and generalized seizures(n=3) were the most common symptoms, and signs encountered. A prothrombotic risk factor was identified in 12 patients.

6. Another study from India by **Brig S Kumaravelu, Maj A Gupta, Brig KK Singh et al.**[85] where Sixty consecutive patients of CVT were managed over a five-year period (2000-2005) in two referral hospitals of the Armed Forces. The age of patients ranged from 5 to 60 years with a mean of 34.97 ± 8.64 years. Majority (75%) of our patients were in 3rd and 4th decades of life. Male female ratio was 11:9. Presenting symptoms were headache in 45 patients, focal neurologic deficits in 38, seizures in 22, fever in 4, jaundice and injury in 2 each. Examination revealed focal neurologic deficits in 51, papilleoedema in 40, meningeal signs in 12 and

concomitant deep vein thrombosis in 10. Eight patients did not have any neurologic deficit. Evaluation of etiological factors revealed puerperium in 16, anemia in 11, meningitis, oral contraceptive use and systemic lupus erythematosus in three each, antiphospholipid syndrome, protein C deficiency and protein S deficiency in two each with one patient showing factor V Leiden mutation. Two patients came from high altitude without any other risk factors. CT scan was normal in 19 patients. Venous hemorrhagic infarcts was seen in 20, nonhemorrhagic infarcts in eight, empty delta sign in eight and diffuse cerebral edema in six cases. Magnetic resonance imaging showed thrombosis of superior sagittal sinus in 44, transverse sinus in 20, straight sinus in 13, sigmoid sinus in nine and cavernous sinus in two patients. Isolated venous infarcts were seen in four patients. Twenty-three patients had hemorrhagic infarcts while nine had nonhemorrhagic infarcts. One patient underwent a four vessel digital substraction angiography that showed superior sagittal sinus thrombosis.

7. In a study **by Wasay et a**l[86] from United states, prospectively and retrospectively 1991-2001 which included 10 centres ., Headache was seen in 129 (71%) Focal motor or sensory deficits in 66

(36%), Nausea/vomiting in 63 (35%),Seizures in 59 (32%), Drowsiness in 51 (28%),Visual blurring in 42 (23%), Slurred speech/inability to speak in (16%), Coma in 27 (15%) and Fever 25 (14%). Neurologic examination findings include Normal neurologic examination result 69 (38%) ,Confusion/drowsiness 55 (30%), Coma in 37 (20%), Dysarthria 37 (20%), Aphasia 9 (5%), Papilledema in 59 (32%), Diplopia in 12 (6%) , Cranial nerve palsies in 33 (18%) Monoparesis in 3 (2%) , Hemiparesis 71 (39%), Paraparesis in 1 ,Ataxia in 25 (14%). According to anatomical localisation of the sinus involved, SSST alone 12 (6%), SSST and TST 9 (5%) SSS and TST 1 St S 2 (1%) and COVT/DCVT 3, SSST with TST with COVT/DCVT 1. Lab investigations showed Systemic lupus erythematosus/ antiphospholipid antibody in 7 (4%), Protein-C deficiency 3 (2%) Protein-S deficiency in 4 (2%), Antithrombin III deficiency in 1, Homocystinemia in 9 (5%), Pregnancy/puerperium 13 (7%) and Malignancy 12 (7%).

8. In a multinational (21 countries), multicenter (89 centers), prospective observational study called international study on cerebral vein and dural venous sinus thrombosis by **Jose M. Ferro et al,**[87] Patients were followed up at 6 months and yearly thereafter. Primary outcome was death or dependence as assessed by modified Rankin Scale (mRS). The study was started in May 1998 and continued until May 2001. Patients were followed up from diagnosis to December 31, 2002. 624 patients were included in the study from 89 centres in 21 countries. In this study headache was present in 88.8%, visual loss in 13.2%, papilledema in 28.3%, diplopia in 13.5 % , stupor or coma 13.9%, aphasia 19.%, aparesis in 37.2 %, bilateral motor signs 3.5 %, focal seizure in 19.6%, seizure with generalization in 30%, Any seizure 39.3%, Sensory symptoms 5.4 %. Risk factors studied showed Thrombophilia in 34.1%, Antiphospholipid antibody in 5.9%, Nephrotic syndromein 0.6%, Hyperhomocysteinemia in 4.5%, Malignancy in 7.4%. Hematological conditions in 12%, Vasculitis in 19.3% , Systemic lupus erythematosus 7.1%, Behçet disease 6.1% Puerperium in 13.8%, Infections in 12.3%, Ear, sinus, mouth, face, and neck 8.2% , Drugs in 7.5%, Radiological features include Superior

sagittal sinus involvement in 62.0%, Lateral sinus- left in 44.7%, Lateral sinus- right in 41.2% , Straight sinus in 18%, Deep venous system in 10.9%, Cortical veins in 17.1% , Jugular veins in 11.9%, Cerebellar veins 0.3%, Cavernous sinus 1.3%.

9. In a study by **Breteau *et al*** [88] from france from 1995-1998, Headache occurred in 30.9%, Focal deficits in 47.3%, Focal or generalized seizures in 50.9%, Impaired consciousness in 18.2%, Decreased visual acuity in 5.5%, Site of sinus occlusion, Superior sagittal sinus occurred in 37%, Lateral sinus in 38%, Straight sinus in 6%. Factors found to cause CVT included Unknown causes in 21.8% , Local infection 5.5%, Cancer 9.1%, Puerperium 5.5%, systemic lupus erythematosus 1% , Crohn's disease 1%, Any coagulation disorder 18.2%, protein C deficiency 2% , Protein S deficiency 4%, Factor V gene mutation 1%, Prothrombin gene mutation 3% and Oral contraceptive use in 52.2%

10. In a study conducted by **Subash Koul et al**[89] in Nizams institute of medical sciences in Hyderabad in India in 2012, males constituted 53.5% mean age of onset was 31.8. Headache was the presenting feature in 94%, vomiting in 74%, seizures in 45%,

hemiparesis in 25%, papilledema in 63%, hyperhomocystinemia was found to be a risk factor in18.2%, alcohol consumption in 15%, protein C in 9%, protein S in 5.1%, ACLA IN 7.2%, infection in 9%, malignancy in 0.9%. Among sinus involvement, SSS along with other sinus involvement was 54.3%, right TS involvement in 31%, left TS in 16%, SG in 20.6%, ST in 4%, deep CVT IN 5.8%, Cavernous sinus thrombosis in 2.4%.

Materials & Methods

METHODS AND MATERIALS

STUDY DESIGN:

Patients with CVT confirmed by imaging studies enrolled in the Dept. Of Neurology from June 2011 to Feb 2013 were included in this study. During the period of admission, patients were evaluated with demographic profile, detailed history with special importance to risk factors like smoking, Alcohol consumption including binge alcohol intake prior to onset of symptoms, substance abuse and clinical examination for various neurological presentations. These patients were evaluated with complete blood count to rule out anaemia/ polycythemia, other blood investigations that are implicated in the pathogenesis of CVT.

STUDY POPULATION:

The study population include male patients who were admitted with acute headache and other neurological features with CT/MRI/MRV (brain) finding of Cerebral Venous Thrombosis in the Department of Neurology, Government Stanley Hospital, and Chennai.

Inclusion Criteria

Patients included in this study were

A. All adult male patients with features of CVT confirmed by CT/MRI brain.

Exclusion Criteria

1. All female patients with CVT.
2. All cases of CVT due to Trauma and neoplastic diseases.
3. Children less than 13 years.

STASTISICAL ANALYSIS

Data was analyzed using SPSS 17.0 Software. Mean for the values were calculated. Variables were compared using Chi-square test a $P < 0.05$ was considered Statistically Significant.

Results

RESULTS

Most of the studies done so far have been for CVT in general including both males and females or had been for puerperal CVT only. Due to the increased case input of male CVT, a prospective observational study was conducted at Department of neurology, Govt. Stanley medical college, Chennai.

1. AGE:

According to the present study, the mean age of onset of CVT in males is 35 years. The range was from 13 years to 63 years. The peak incidence occurred in the age group of 21-25 and 31-35.

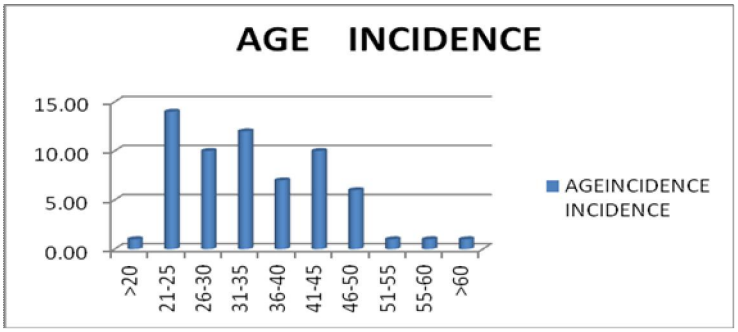


Figure 1 – Age Incidence of CVT

Table 1: Age Incidence of CVT

AGE (yrs)	>20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	55-60	>60
INCIDENCE	1	14	10	12	7	10	6	1	1	1

2. RISK FACTORS:

Smoking and alcohol were noted as risk factors, both were present in 82% of the individuals. History of binge alcohol was present in most of the patients.

Table 2: Smoking and Alcohol as risk factors

Parameters	Present (n)	Percentage	Absent (n)	Percentage
Smoking	49	82%	11	18%
Alcohol	49	82%	11	18%

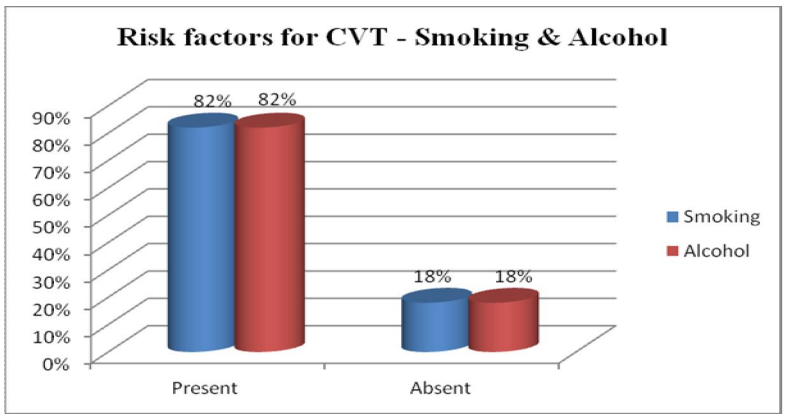


Figure 2: Risk factors for CVT – Smoking & Alcohol

3. CLINICAL MANIFESTATIONS

A. Headache:

Headache was the most common clinical manifestation noted in our patients. All of our patients (100%) presented with headache.

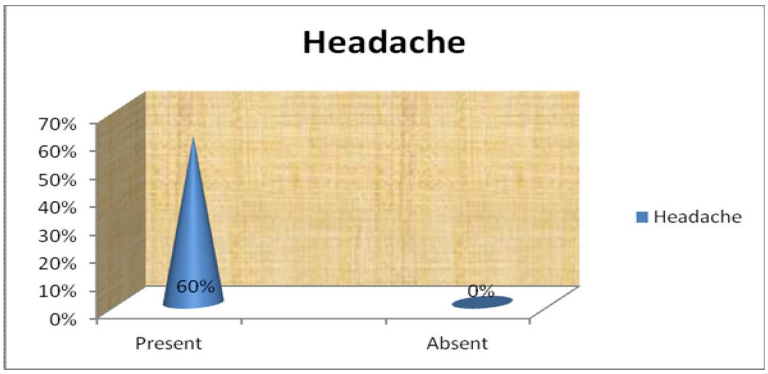


Figure 3: Headache

B. Vomiting:

Vomiting was present in 65% o the patients.

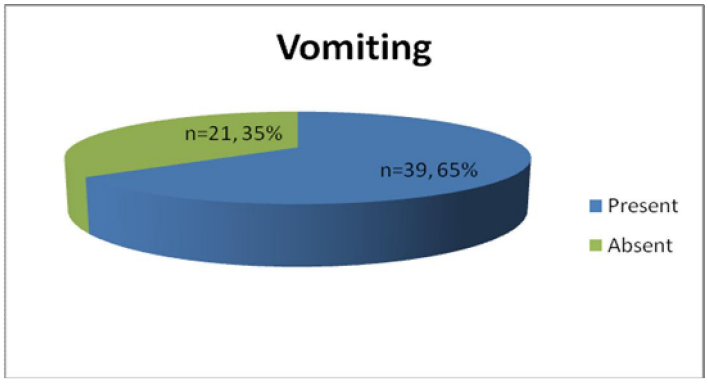


Figure 4: Vomiting

C. Seizures:

Seizures was present in 80% of the patients, both generalised and focal seizures were noticed.

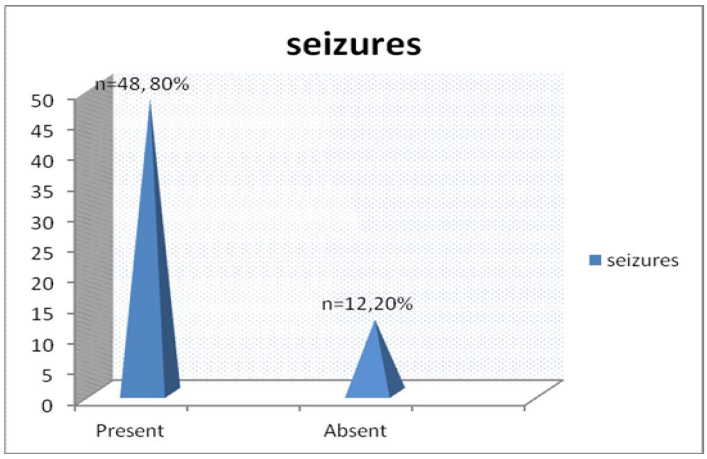


Figure 5: Seizures

Table 3: Symptoms

Headache	60	100%	0	0%	**60**
Vomiting	39	65%	21	35%	**60**
Seizures	48	80%	12	20%	**60**

D. DIPLOPIA

Diplopia was present in 37% of patients. This was due to either lateral rectus weakness due to raised ICT and due to the involvement of multiple cranial nerves in cavernous sinus thrombosis. Patients with papilledema also had blurring of vision.

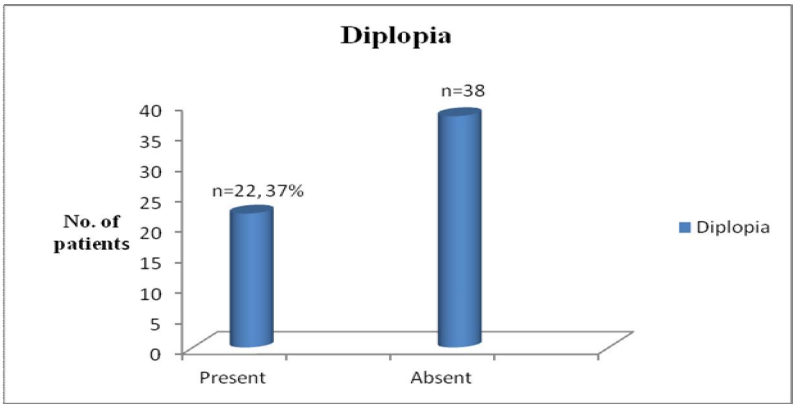


Figure 7: Diplopia

E. PAPILLEDEMA:

Papilledema was present in 40% of patients

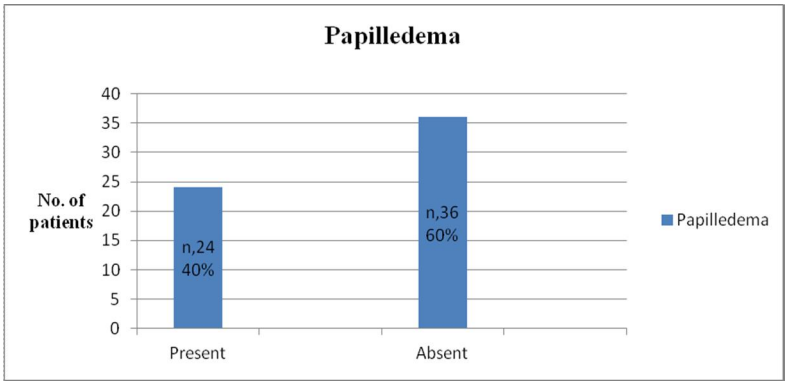


Figure 8: Papilledema

F. FOCAL MOTOR DEFICITS

Foal motor deficits in the form of hemiparesis or monoparesis was present in 47% of the patients. Most of them recovered following treatment. 15% had a residual weakness.

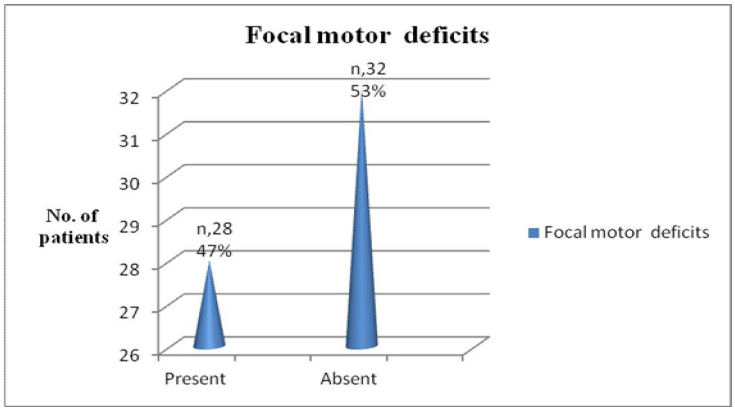


Figure 9: Focal motor deficits

G. Aphasia

Aphasia was one of the presenting feature in 13% of the patients .Motor aphasia was the most common form noticed.

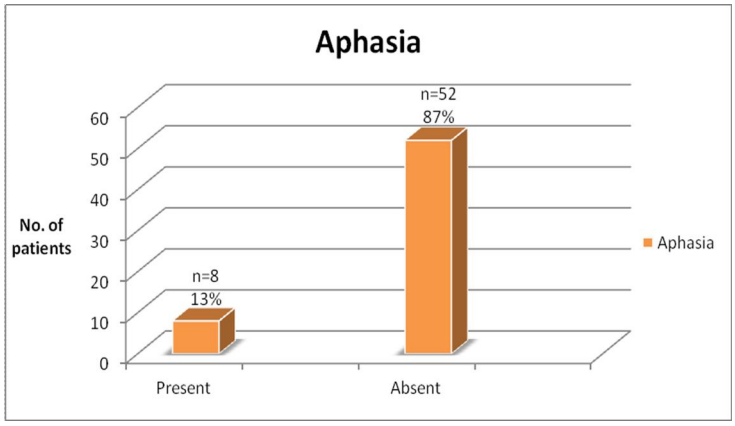


Figure 10: Aphasia

Table 4: Signs

Parameters	Present		Absent		Total
	No. of patients	%	No. of patients	%	
Aphasia	8	13%	52	87%	**60**
Hemiparesis	28	47%	32	53%	**60**
Papilledema	24	40%	36	60%	**60**
Diplopia	22	37%	38	63%	**60**

LAB PARAMETERS

Table 5: Prothrombotic workup

Parameters	Negative		Positive		Total
	n	%	n	%	
ANA	50	83%	10	17%	**60**
LA	59	98%	1	2%	**60**
Anti Cardiolipin Ab	57	95%	3	5%	**60**
Protein C	60	100%	0	0%	**60**
Protein S	60	100%	0	0%	**60**
Antithrombin III	58	97%	1	2%	**60**

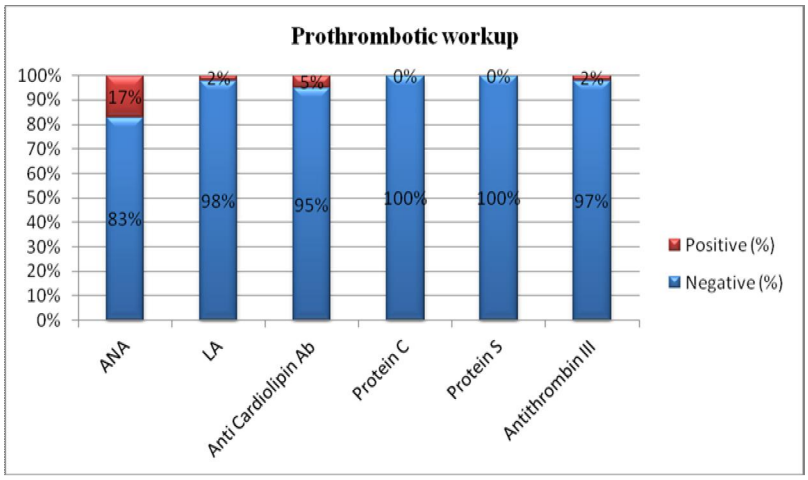


Figure 11: Prothrombotic workup

ANTINUCLEAR ANTIBODY

Anti nuclear antibody was positive in 10 of our patients which comprised 17%.

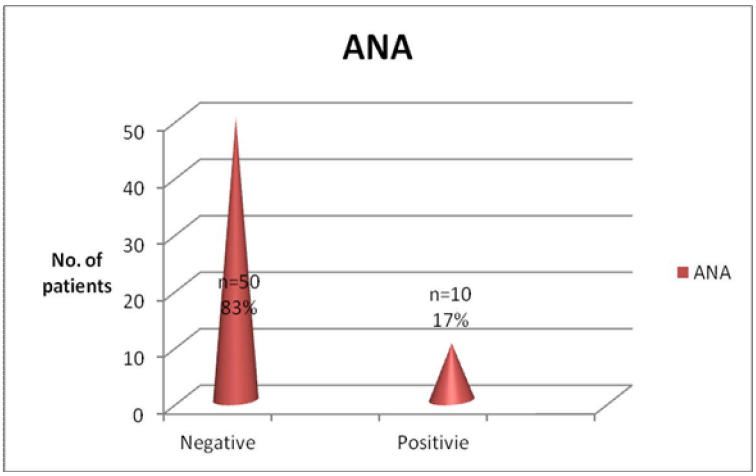


Figure 12: ANA in CVT

LUPUS ANTICOAGULANT (LAC)

LAC was positive in only one of our patient

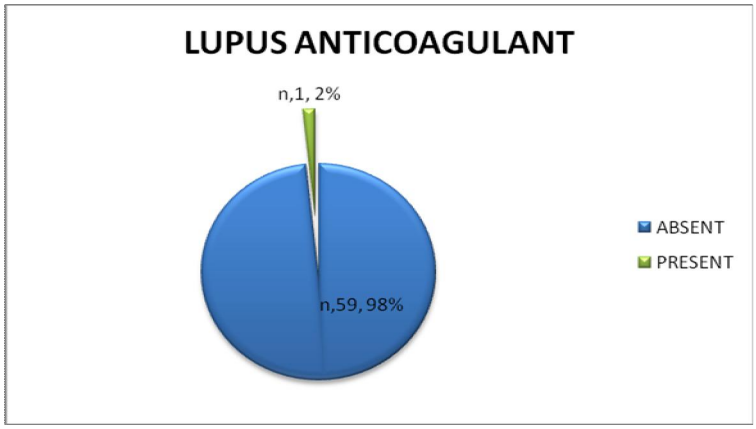


Figure 13: LUPUS ANTICOAGULANT

ANTICARDIOLIPIN ANTIBODY (ACA)

ACA was positive in three of our patients.

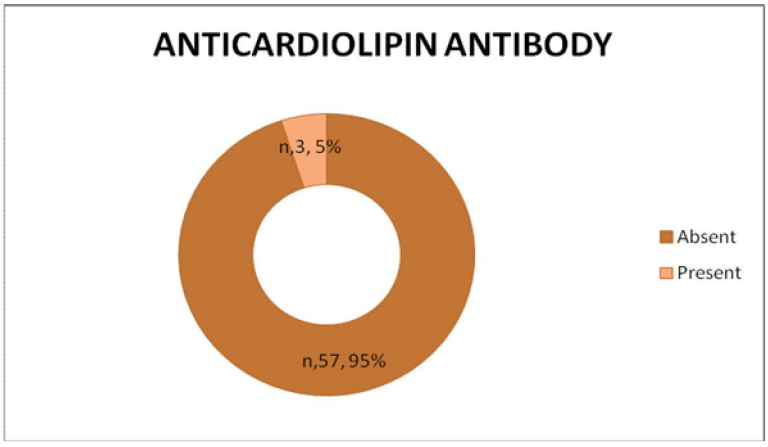


Figure 14: ANTICARDIOLIPIN ANTIBODY

ANTI THROMBIN III DEFICENCY

Antithrombin III deficiency which is a risk factor for hypercoagulable state was positive in one of our patient.

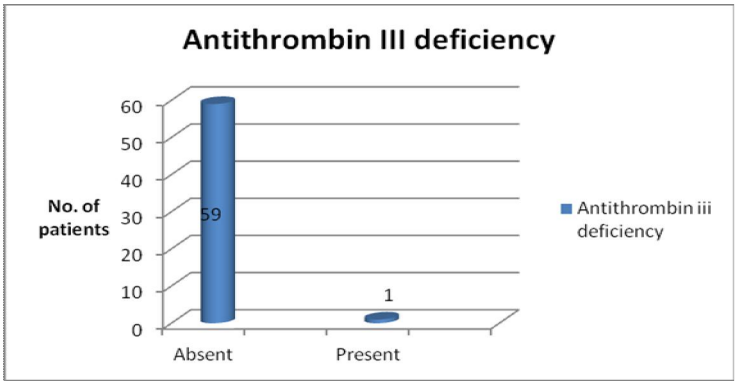


Figure 15: Antithrombin III deficiency

SERUM HOMOCYSTEINE LEVEL

Table 6: Homocysteine level in CVT

Parameters	ELEVATED	NORMAL
Homocysteine	35	25

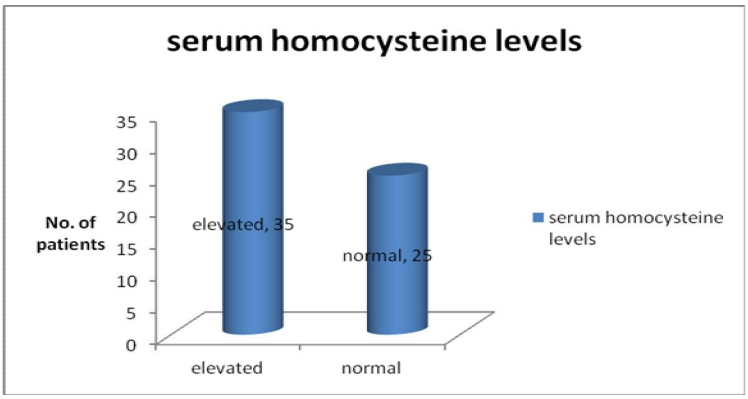


Figure 16: Homocysteine level

Serum homocysteine levels were elevated in 35 of our patients totally. Of these 35, 32 patients were alcoholics, with a history of binge alcohol in most of them. Only three patients were non alcoholics.

With these values hyperhomocystenemia can be considered as an important cause of the hypercoegulable state which might be contributory to the pathogenesis of CVT in this subset of patients.

CHI-SQUARE TEST-ALCOHOL AND SERUM HOMOCYSTEINE LEVELS

Table 7

Alcohol Consumption	**Elevated**		**Normal**		**Total**	χ^2	**P-Value**
	n	**%**	**n**	**%**			
Absent	3	27%	8	73%	**11**	5.346	0.021*
Present	32	65%	17	35%	**49**		

Chi –square test computed on values of homocysteine and alcohol showed a significant p value between the two indicating a stastically significant association between the two.

INCIDENCE OF SINUS INVOLVEMENT

Table 8: Incidence of Sinus involvement

Parameters	SSS	TS	SG	HE	DEEP	CAV
N	43	26	16	18	9	2
%	72	42%	23%	30%	15%	3%

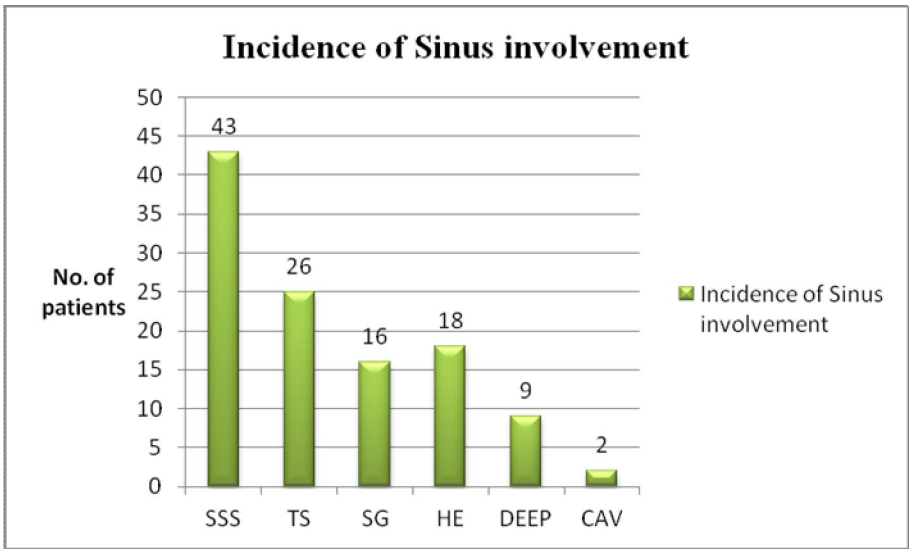


Figure 17: Incidence of Sinuses involvement

The most common sinus involved is the superior sagittal sinus 43(72%) patients presented with superior sagittal sinus involvement either alone or in combination. Out of the 43, I5 SSS involvement alone. 13 had associated transverse sinus involvement also. One patient had involvement of SSS and Sigmoid sinus involvement. Deep vein thrombosis along with SSS was noticed in 2 patients. SSS with TS with SG involvement occurred in 5 patients. In SSSS thrombosis,

haemorrhage occurred in 9 patients in which 2 had associated SAH (Subarachanoid haemmorage). Two patients were associated with SAH alone.

Table 8: Multiple sinus involvement with SSS

Sinus Involvement	SSS	SSS+TS	SSS+SG	SSS+TS+SG	SSS+TS+SG +HE	SSS+TS+HE	SSS+HE	SSS+DEEP	SSS+SAH
No. of patients	28	13	1	6	2	1	11	4	4

Transverse sinus (TS) involvement either alone or in combination with other sinus involvement occurred in 26 of the patients. Out of the 26 patients, 13 had thrombosis of TS+SG. 2 patients had TS+SG+ haemmorhage. Only 2 patients had isolated TS with haemorrhage

Table 9: Transverse sinus involvement

Sinus Involvement	TS ALONE	TS+SSS+SG	TS+SG	TS+SSS+SG	TS+SSS	TS with all sinuses
No. of patients	4	9	9	6	13	26

Deep CVT was present in 9 of the patients. 8 out of 9 patients had associated superior sagittal sinus thrombosis. Only 1 patient with

transverse sinus involvement had associated deep sinus thrombosis. 2 out of the 9 patients with deep CVT died.

OTHER ASSOCIATIONS IN MRI-BRAIN

Table 10: Associated Lesions

Parameters	Present		Absent		Total
	n	%	n	%	
Sinusitis	8	13.3%	52	86.7%	**60**
Granulomas	1	2%	59	98%	**60**
Carcinoma related	2	4%	58	96%	**60**

Other associated features in the imaging included sinusitis, mastoiditis, granuloma and carcinoma related findings.

SINUSITIS

Sinusitis was present in 8 out of 60 patients.

MASTOIDITIS

Mastoiditis is present in 6 patients. All 6 patients had transverse sinus thrombosis either alone or in combination with other sinus involvement.

Fishers' exact test showed an extreme significance stastistically for this association.

Table 12: Association between TS and Mastoiditis

TS/ Mastoditis	Absent		Present		Total	χ^2	P-Value
	n	%	n	%			
Absent	34	100%	0	3%	**34**	43.619	<0.001*
Present	20	77%	6	20%	**26**		

GRANULOMA

One patient had an associated granuloma with sinus thrombosis. He had a high parietal infarct with superior sagittal sinus thrombosis along with haemorrhage

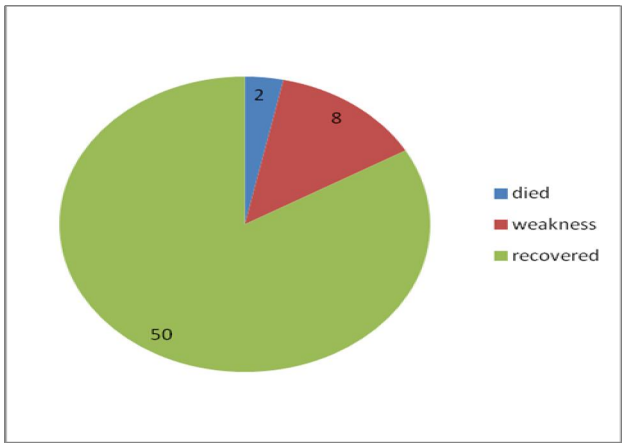
CARCINOMA

Two patients had thrombosis adjacent to carcinomatous condition. One patient had an embryonal rhabdomyosarcoma abuting the left

sigmoid and transverse sinus. The other patient had thrombosis of the right internal jugular vein due to destruction of wall of jugular foramen due to metastasis.

PROGNOSIS

Out of 60 patients in the study, 2 patients died , 8 patients had persistent neurological deficit. The rest improved (50= 83%)



Discussion

DISCUSSION

The present study has been conducted at Stanley medical college in Chennai. Stanley medical college caters a major part of north Chennai, whose inhabitants are mostly manual labourers. Alcoholism is very rampant in this part of the city, which is the area where harbour is located. Hence handling of goods and cargo is the major occupation of the men in this area which is the reason given by the inhabitants as a reason for increased alcohol consumption. Women alcoholics are also common here and women getting admitted in the medical gastroenterology ward for alcoholic liver disease are not uncommon.

An earlier study of cerebral venous sinus thrombosis done in the department of medicine in 2010 in Stanley Medical College showed a higher incidence of CVT in males in contrast to studies available at that time. Hence this study was exclusively done in male patients to try to find a possible etiological background for the increased incidence of CVT in males in this part of the country with the possible available resources in a government hospital set up.

Males to female ratio in various studies like Mohammed najib et al.[84], santo gr et al., Vembu et al.[80] is favouring a female preponderance.

But in studies by kumaravelu et al.[85] and by Subash Kaul et al.[89] (both studies from India) there is a male preponderance.

AGE

Age of incidence varied from 13 years to 63 years in the study. The study did not include paediatric patients. Hence children below 13 years were not included in the study. Average age of onset was 35 years with a peak incidence in the third and fourth decade. The results were consistent with the other studies by Subash kaul et al. [89], Algatani et al.[83], Mohammed najib et al.[84] and Brig. S.Kumaravelu et al.[85] which also have similar age incidence. But all the available data are only for CVT in common and not for male CVT alone.

RISK FACTORS

Smoking and alcoholism can be considered as a risk factor according to this study. 82% of patients were smokers and/or alcoholics. H/O substance abuse was present in many patients but since the substance abused were native substances whose composition was not known, so it was not included in the study. But the possible contribution to the hypercoagulable state by these substances cannot be ignored. The chemical components of these substances are not constant. Hence it is

assumed that their contribution to the hypercoagulable state by these substances could be significant and it needs a separate study.

CLINICAL FEATURES

SYMPTOMS

Headache is the cardinal symptom noted in the study. All patients had a history of recent-new onset headache. 100% of patients had headache at presentation. Head ache as a presenting feature was present in 93% in a study by Vembu et al.[80], in 82% in Abdulkader Daif et al.[81], 100% in a study by Mohammed Najib et al.[84], 75% in a study by Brig. S. Kumaravelu et al.[85], 71% in a study by Wasay et al.[86], 88% in ISCVT, [87] 30.9 in Breteau et al.[88], NIMS study 94%.[89]

Vomiting was present in 65%, of our patients. In the study by Wasay et al.[86], vomiting was found in 35% of patients and in the NIMS study[89] vomiting was present in 74% of the patients.

Diplopia / blurring of vision was present in 37% of our patients. Though blurring of vision was the predominant complaint, diplopia was also seen in patients with features of increased intracranial tension and in patients with cavernous sinus thrombosis who had cranial nerve

palsies. Blurring of vision was present in a study by Wasay et al.[86] 23.1%, ISCVT[87] in 13.5%, Breteau et al, [88] 5.5%

Seizure is a manifestation in 80% of our patient's. They were both focal and generalised. Seizure was present in 31% in a study by Vembu et al.[80], 10% in the study by Abdul Kader et al.[81], 36% in the study by Brig. S. Kumaravelu et al, [86] 39.3% in ISCVT[87], 50.9 % in the study by Breteau et al.[88], and 45% in the NIMS study[89].

A wide degree of variation has been noted in the incidence of seizures among the various studies- our study showing the highest incidence. The high incidence of seizures in our study can be attributed to multiple causes. The high prevalence of alcoholism in our patients could itself be a cause of seizures – seizures could either be a rum fits secondary to binge alcohol intake, or due to a withdrawal state following the symptoms of headache and generalised ill health noted by the patient, which might have led to him acutely withdraw the alcohol which might have caused a withdrawal seizures. The presence of multiple sinus thrombosis and an extensive involvement of these, with a resultant haemorrhage may be causative factors for seizures in these patients.

SIGNS

PAPILLEDEMA

The incidence of papilledema in our study was 40%. In other studies varies from 28% to 86%. In ISCVT[87] the incidence is 28.3% , 28% in a study by Vembu et al.[80] , 80% in the study by Abdulkader et al.[81], 86% in the study by Mohammed Najib et al.[84], 66% in the study by Kumaravelu et al.[85], 32% in Wasay et al.[86], and in the NIMS study[89] it was 63%.

APHASIA

13% of our patients develop aphasias. The speech difficulties varied from slurring of speech to pure aphasias. Deepening on the site and side of the infarct or haemorrhage, the presentation varied. In the ISCVT[87], aphasia was present in 19% of the patients. In the study by Wasay et al.[86] the incidence of speech abnormality was 16%. The incidence of speech abnormalities coincides with our data too.

FOCAL NEUROLOGICAL DEFICIT

47% of our patients had focal neurological deficits in the form of monoparesis, hemiparesis or cranial nerve palsies. The range of foal

deficits varied in different studies from 25% to 66%. It was 25% in the NIMS study[89], 27% in Abdul kaders et al.[81] study, 37% in the study by Vembu et al.[80], 63% in Brig. S.Kumaravelu et al.[85], 66% in the study by Wasay et al.[86], 37.2% in ISCVT[87] and 47.3% in the study by Breteau et al.[88]

LAB PARAMETERS

Prothrombotic states considered in the study included serum ANA, Lupus anticoagulant, Anticardiolipin antibody, Antithrombin III, Protein C, Protein S, and Serum homocysteine levels. ANA was positive in 17% of our patients. In other studies, ANA was positive in 7% of patients in the study by Abdul Kader et al.[81],5% in S.Kumaravelu et al.[85],4% in Wasay et al.[86], and 7% In ISCVT.[87]

Anti Thrombin III was positive in 2% of our patients. In the study by Wasay et al.[86], it was positive in 1% of his patients.

Protein C and Protein S deficiency was not present in our study. Lupus anticoagulant was present in 2% of our patients. Anticardiolipin antibody was present in 5% of our patients.

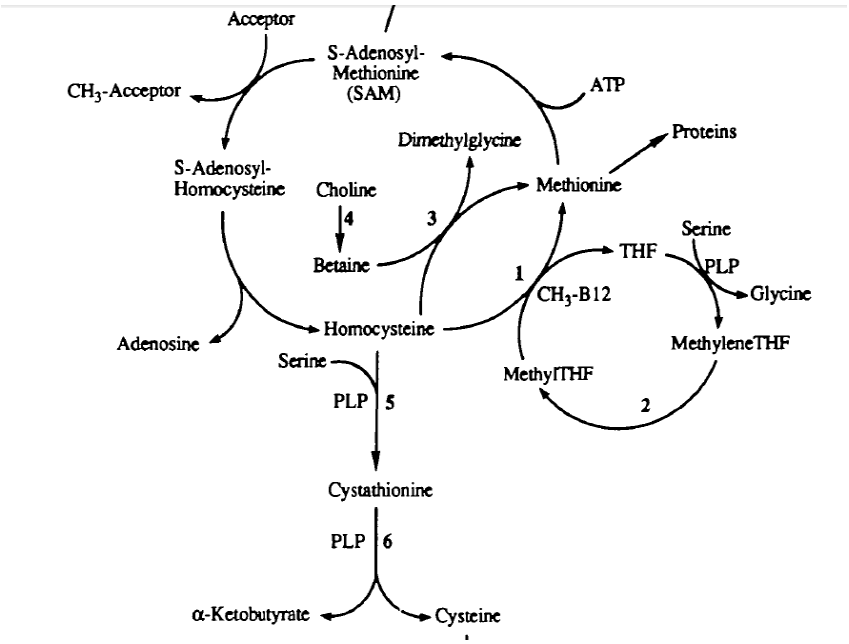
Serum Homocysteine levels were elevated in 55% of our patients. In other studies it was not so much elevated. Elevated homocysteine was

studied in three other studies. In the study by Wasay et al.[86] the it was elevated in 5% of the patients. In the ISCVT[87] hyperhomocystenemia was present in 7% of the patients. In the study from NIMS[89], hyperhomocystenemia was present in 18% of the patients. Chi –square test computed on values of homocysteine and alcohol showed a significant p value between the two indicating a statically significant association between the two in our study.

HOMOCYSTEINE ELEVATION IN ALCOHOLICS

Homocysteine is a thiol containing aminoacid which is derived from the aminoacid methionine. It is produced entirely from the methylation cycle as it is absent in the dietary sources. Homocysteine is remethylated to methionine. This conversion is catalysed by methionine synthese or by transsulphuration to cysteine. The latter reaction is catalysed by cystathionine β synthese.vitamin B-12, B-6 are eassential co-factors and folic acid is an essential co-substrate for the remethylation of homocysteine. It is plausible that the tissue folate concentrations are closely associated with regulation of homocysteine metabolism and homocysteine concentration bear an inverse correlation with the above vitamins[90].

Figure 21: METABOLISM OF HOMOCYSTEINE



In a study by Bleich et al[90],it was found , in patients with alcohol intake , the levels of homocyteine was elevated and levels of folic acid was decreased. They also documented a gradual decrease in homocysteine levels in the following week with withdrawal of alcohol. They also postulated that the alcohol withdrawal symptamatology is due to the to the increased levels of aspartate and glutamate along with their sulpanated derivative –homocyteic acid and cysteine sulphinic acid along with upregulation of NMDA receptors result in excito toxicity which result in the withdrawal symptoms.

In a study by Robert M Russel et al.[91], the increased urinary excretion during ethanol ingestion was documented using radio labelled studies. In another study by Charles H Halsted et al.[92], it was documented by radiolabelled studies that there is a decreased jejunal intake of radiolabelled folate in alcoholic patients.

In a study entitiled hyperhomocysteinemia in cerebral venous thrombosis by Ida Martinelli et al.[93] it was found that patients with hyperhomocysteinemia had a 4 fold risk of cerebral venous sinus thrombosis.

With the above references, hyperhomocystenemia which has been present in 55% of our patients could be secondary to the high incidence of alcoholism and binge alcohol intake in the study group. The alcohol related derangements in folate metabolism could be the reason for hyperhomocystenemia in our patients manifesting as cerebral venous sinus thrombosis.

ASSOCIATED LESIONS CAUSING CVT

Mastoiditis was documented in MRI Brain in 10%. Granuloma was associated as cause of the adjacent cortical veins thrombosis resulting in the thrombosis of the adjacent SSS resulting in haemorrhagic infarct in one patient.

Sinusitis was associated with cavernous sinus thrombosis in one patient. Another patient with cavernous sinus thrombosis which was a recurrent episode did not have sinusitis in imaging, but had hyperhomocystenemia.

2 (3.3%) of the patients had thrombosis in sinuses adjacent to a malignant infiltration. One patient had a lesion suggestive of an embryonal cell carcinoma in the left mastoid bone with thrombosis of the left sigmoid sinus. The other patient had a lesion suggestive of a metastasis in the right jugular foramen and thrombosis of the contiguous right jugular foramen and sigmoid sinus. Quoting other studies, the incidence of malignancy was 7% in abdulkader et al.[81], 7% in study by Wasay et al.[86], 7.4% in ISCVT[87], 9.1% in Breleau et al.[88] and 0.9% in the NIMS study[87]. The varied incidence may be due to availability of specialised oncological units which is not present in our institution.

ANATOMICAL LOCALISATION IN IMAGING

All of our patients were subjected to MRI brain with MR Venogram, MR angiogram, diffusion weighted sequences and ADC mapping and gradient echo sequences.

The anatomical localisation of the sinus involvement is as follows:

The superior sagittal sinus (SSS) was involved along with other sinus in 43 (72%) patients. SSS was involved alone in 28 patients (46%). SSS was involved along with transverse sinus (TS) in 13 patients (21.6%). SSS was associated with TS and sigmoid sinus (SG) in 6 patients (10%). SSS is present with deep vein thrombosis in 8(13.33%) SSS was associated with haemorrhage/haemorragic infarct in 11 patients(18.3%). 4 patients had subarachanoid haemorrhage associated with SSS thrombosis- out of which two were associated with haemorrhage and two had isolated SAH. SSS involvement along with TS with sigmoid sinus (SG) and haemorrhage is present in 2(3.3%). SSS is associated with transverse sinus with haemorrhage in 1 pt (1.6%).

Transverse sinus (TS) involvement is present in 26 patients (43.3%) together along with other sinus involvement. Isolated TS thrombosis is present in 4 patients (6.6%). TS is associated with SG in 9 (15%) patients. TS is associated with deep venous sinus thrombosis in 3(5%) patients.TS is associated with haemorrhage in 6 patients (10%).

Mastoiditis is present in 6 patients (10%). All patients with mastoiditis have associated tranverse sinus thrombosis. The fishers exact table was used to find out association between mastoiditis and transverse sinus involvement. The test has a stastistically significant

association between the two with a p-value of < 0.0001 postulating a strong association between the two.

Sigmoid sinus involvement is present alone in only one patient. With other combinations it is present in 19 patients (31.6%). SG and TS sinus involvement is present in 11 patients (18.3%)

TS +SSS+SG is present in 5 patients. SG thrombosis is present with IJV thrombosis in one patient with metastatic lesion in the jugular foramen. SG +SSS+ Deep system +haemorrhage is seen in one patient, SG+SSS+Deep vein thrombosis is noted in one patient.

Cavernous sinus thrombosis is present in 2 of our patients (3.3%) one patient was associated with sinusitis and in other patient sinusitis could not be documented. But in the second patient hyperhomocystenemia was a risk factor.

Deep vein thrombosis is present in 9 (15%) of patients. 8 (13.3%) had associated SSS thrombosis also. 4 patients had a combination of SSS+TS+ DEEP vein sinus thrombosis. 2 patients with extensive CVT with deep vein thrombosis who presented with GCS less than 8, died.

Haemorrhage is present in a total of 18 (30%) of patients. SSS is associated with haemorrhage in 11 patients. Haemorrhage is associated

with TS in 6 (10%) of patients. Deep CVT is associated with haemorrhage in 5 patients (8.33%). Subarachanoid haemorrhage (SAH) was associated in 4 patients .of the 4, 2 had associated haemorrhage, but the remaining two were associates with SAH in the presence of SSS thrombosis. SAH is not a common manifestation in CVT. It is postulated to the rupture of cortical veins abutting the surface which results in SAH.

Table 13: Site of CVT in various studies

Sinus involved	Vembu et al.[80]	Brig. S.kumaravelu et al.[85]	Wasay et al.[86]	ISCVT[87]	NIMS STUDY[89]	Present study
SSS	59%	73%	62%	37%	37.3%	72%
TS	54%	33.3%	-	18%	47%	43%
SG		3.3%			20%	31%
CAV				1.3%	2.4%	3%
Deep CVT				11%	5.8%	15%
Haemorrhage	18%	15%				30%

PROGNOSIS

Out of 60 patients in the study, 2 patients died, 8 patients had persistent neurological deficit. The rest improved (50= 83%).

Conclusion

CONCLUSION

Cerebral venous thrombosis (CVT) which was previously thought to be an uncommon condition is now being diagnosed frequently due to increasing awareness and improvement in imaging modalities. Cerebral venous sinus thrombosis presents with a wide variety of clinical manifestation, the most common being acute onset headache, seizures, features of raised intracranial tension and focal neurological deficits not pertaining to arterial territorial region.

Thrombophilic conditions and hyper oestrogenic states in a setting of dehydration are known factors postulated in the causation of CVT. This study, exclusively done in male patients is the first of its kind to our knowledge from the literature. From the results obtained in this study, alcoholism, which is very much rampant in this part of Chennai, seems to be cause for the higher incidence of CVT in males. The correlations of the various studies quoted from the literature, makes it plausible to consider folate deficiency in alcoholics with the resultant hyper homocystinemia as the cause for the hyper coagulability. Further, in our study group which includes people who are manual labourers, belonging to low socioeconomic class, pre-existent nutritional

deficiency might also contribute to the clinical scenario. Hence these nutritional deficiencies, which are amenable for correction, if sought earlier and corrected in the high risk group, might decrease the incidence of this catastrophic disease.

Further large scale studies are needed to establish a clear relationship between these factors in our population. Studies are also needed in the context of treatment with folic acid, methyl cobalamine, and pyridoxine in the acute setting of CVT. Further studies are also needed in pregnant and the puerperal women who will also have decreased folate levels due to increased demand. The appropriate dose of folic acid needed to overcome these deficient states in various population subgroups needs to be quantified by further studies.

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Annexure I–Proforma

STUDY OF CEREBRAL VENOUS THROMBOSIS IN MALES

PROFOMA

Name : Age : Sex :

Occupation : Address : Ip No. :

Ward :

Neuro No.

Date of admission : Date of Discharge :

Socioeconomic status:

1. History of presenting neurological illness
   A. H/o Headache, Seizures
   B. Prior H/o Fever, Vomiting, Diarrhoea
   C. Motor/sensory/cranial nerves/cerebellar/bladder symptoms.
   D. Symptoms of increased intracranial pressure
   E. Symptoms of meningeal irritation

2. Past history
   Hypertension / diabetes mellitus / coronary heart disease /
   dyslipidemia / Deep vein thrombosis / connective tissue disorders /

3. Personnel history

   Smoking/Alcohol/Substance abuse (cocaine)

4. Family history

   Stroke / Diabetes / Hypertension

   Hypercoagulable state

5. Drug history

6. General examination

   Pulse rate: Blood pressure: lying : right left

   Temperature:

   Respiratory rate:

   Pallor/polycythemia:

   Hydration:

7. Central nervous system examination:

   Consciousness / Glascow coma scale

   Pupil size, reaction to light.

   Cranial nerve examination including fundus.

   Examination of motor / sensory / cerebellar system to localize the level of lesion meningeal signs

8. Other systems:

CVS : first and second heart sounds / murmurs

RS : breath sounds

ENT : Paranasal sinus / Mastoid tenderness

9. Investigations:

1. Haemoglobin, total count, differential counts
2. ESR
3. Coagulation profile
4. Blood sugar – random, if high - fasting and 2hour postprandial
5. Urea / creatinine
6. Electrolytes
7. Lipid profile
8. HIV – I & II
9. ANA(if positive ds DNA), APLA, ACLA, Sr.Homocysteine, Sr.Fibrinogen,
10. Thyroid Function Test
11. X-Ray paranasal sinus/ ENT opinion
12. Electrocardiogram
13. Chest x ray
14. CT Brain with Contrast / MRI brain / MRV

Annexure ***II*** *– Master Chart*

S. No	Name	Age	Sex	IP/OP no	Smo-king	Alco-hol	Head ache	Vomi-ting	LOC	Fits	Dys-phasia	Hemi-paresis	PAP	GCS	BP	ANA	LA	Anti Cardio-lipin Ab	Homo-cysteine	Protein C	Protein S	Antith-rombin III	MRI										Prog-nosis
																							SSS	TS	SG,IJV	HE	DEEP	CAV	MASTO-IDITIS	Sinu-sitis	Granu-lomas	Carci-noma related	
1	KUMERESAN	28		1924/11	N	N	Y	Y	N	Y	Y	Y	Y	13		N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
2	VINOTH	25		4536/11	Y	Y	Y	Y	N	N	N	N	N	15		N	N	N	N	N	N	N	SSS	N	N	A	N	N	N	N	N	N	W
3	ANTONY RAJ	35		5554/11	Y	Y	Y	N	N	Y	N	Y	Y	15		N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
4	SURESH	24		5754/11	Y	N	Y	Y	N	Y	N	N	N	15		N	N	N	E	N	N	N	SSS	N	N	SAH	N	N	N	N	N	N	R
5	SUBRAMANIUM	50		8871/11	Y	N	Y	Y	N	N	N	N	N	15		N	N	P	N	N	N	N	SSS	N	N	A	N	N	N	N	N	N	W
6	PARTHIBAN	24		7680/11	Y	Y	Y	Y	N	Y	N	N	N	15		N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
7	AMALRAJ	25		8765/11	Y	Y	Y	Y	N	Y	N	Y	Y	15		N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
8	KRISHNAN	29		9452/11	Y	Y	Y	N	N	N	N	N	N	15		N	N	N	N	N	N	N	SSS	N	N	P	N	N	N	N	N	N	W
9	MASTHAN	25		10561/11	Y	Y	Y	N	N	Y	N	N	N	15		N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
10	NAGAPPAN	45		672/12	Y	Y	Y	Y	N	Y	N	Y	N	15		N	N	N	E	N	N	N	SSS	TS	N	A	N	N	N	Y	N	N	R
11	BALAKRISNAN	32		953/12	Y	Y	Y	Y	Y	Y	N	Y	Y	8		P	N	N	E	N	N	N	SSS	N	N	A	P	N	N	N	N	N	D
12	MURUGAN	27		1127/12	Y	Y	Y	N	N	N	N	N	N	15		N	N	N	N	N	N	N	N	TS	SG	A	N	N	N	Y	N	N	R
13	KRISHNAMOORTHY	26		1092/12	Y	Y	Y	Y	Y	Y	N	Y	Y	3		N	N	N	E	N	N	N	SSS	N	SG	P	P	N	N	N	N	N	D
14	SIRANJEEVI	34		1673/12	Y	Y	Y	N	Y	Y	N	Y	Y	10		P	P	P	N	N	N	N	N	TS	SG	P	N	N	N	Y	N	N	W
15	NMANIKANDAN	35		2866/12	Y	Y	Y	Y	N	Y	Y	Y	Y	14		P	N	P	E	N	N	N	N	TS	N	A	N	N	N	Y	N	N	W
16	RAGUPATHY	42		2943/12	Y	Y	Y	Y	N	N	N	N	N	15		N	N	N	N	N	N	N	N	TS	N	A	N	N	N	Y	N	N	R
17	PANDIAN	47		1983/12	Y	Y	Y	Y	N	Y	Y	Y	Y	14		N	N	N	E	N	N	N	SSS	N	N	A	P	N	N	N	N	N	W
18	DASS	43		3079/12	Y	Y	Y	Y	N	Y	N	N	Y	15		N	N	N	E	N	N	N	SSS	TS	N	P	N	N	N	N	N	N	R
19	HUSSAIN	40		3274/12	Y	Y	Y	Y	N	Y	N	Y	N	14		N	N	N	E	N	N	N	SSS	TS	N	P	N	N	N	Y	N	N	R
20	BALAIAH	63		3592/12	Y	N	Y	N	N	N	N	N	N	15		N	N	N	N	N	N	N	N	N	SG,IJV	A	N	N	N	N	N	Y	R
21	PRAKASH	35		3853/12	Y	Y	Y	Y	N	Y	N	N	Y	15		N	N	N	N	N	N	N	SSS	TS	N	A	P	N	N	Y	N	N	R
22	RAJENDRAN	40		4741/12	N	N	Y	Y	N	Y	N	N	N	15		N	N	N	N	N	N	N	SSS	TS	N	A	N	N	N	Y	N	N	R
23	NAGAPPAN	45		4603/12	Y	Y	Y	Y	Y	Y	N	N	Y	14		N	N	N	E	N	N	N	SSS	N	N	A	P,	N	N	N	N	N	R
24	SAKTHIVEL	35		5496/12	Y	Y	Y	Y	N	Y	N	Y	Y	14		N	N	N	E	N	N	N	N	TS	SG	P	N	N	N	Y	N	N	W
25	DHOMADHARN	44		5597/12	Y	N	Y	Y	N	N	N	N	N	14		N	N	N	N	N	N	N	SSS	TS	SG	A	N	N	N	Y	N	N	R
26	THIRUNAVUKARASU	46		5876/12	Y	Y	Y	Y	Y	Y	N	N	Y	15		P	N	N	E	N	N	N	SSS	N	N	A	P	N	N	Y	N	N	R
27	SAHUL HAMEED	45		6234/12	Y	Y	Y	Y	N	Y	N	N	N	14		N	N	N	E	N	N	N	N	N	SG	A	N	N	N	Y	N	N	R
28	MOORTHY	38		6573/12	Y	N	Y	Y	N	Y	N	N	N	15		N	N	N	N	N	N	N	N	N	N	A	N	N	P	Y	N	N	R
29	SHANMUGAM	55		6732/12	Y	Y	Y	Y	N	Y	N	N	N	13		N	N	N	N	N	N	N	N	TS	N	A	N	N	P	Y	N	N	R
30	VIKRAM	26		6582/12	N	Y	Y	Y	N	Y	N	N	N	15		N	N	N	E	N	N	N	N	TS	SG	A	N	N	P	Y	N	N	R
31	MAHESH	36		6798/12	Y	Y	Y	N	N	Y	N	N	N	15		P	N	N	E	N	N	N	SSS	TS	N	A	P	N	N	Y	N	N	R
32	SADHIQ	24		6990/12	Y	Y	Y	Y	N	Y	N	N	N	14		N	N	N	E	N	N	N	SSS	N	N	P	P	N	N	N	N	N	R
33	TAMILSELVAN	50		5702/12	Y	Y	Y	Y	N	Y	N	Y	Y	15		N	N	N	N	N	N	N	SSS	TS	SG	A	N	N	P	Y	N	N	R
34	OMAL	13		6519/12	N	N	Y	Y	Y	Y	N	Y	Y	13		N	N	N	N	N	N	N	SSS	TS	N	A	N	N	N	N	N	N	R
35	KALAIVANNAN	27		8210/12	Y	Y	Y	Y	N	N	N	N	N	15		P	N	N	N	N	N	N	N	TS	IJV	A	P	N	N	N	N	Y	R
36	SULTHAN	37		7945/12	Y	Y	Y	N	N	Y	N	Y	N	13		N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R

37	ELONGOVAN	25		7631/12	Y	Y	Y	N	N	Y	N	Y	N	14	P	N	N	E	N	N	N	N	TS	SG	A	N	N	P	Y	N	N	R
38	VINOTH KUMAR	30		4762/12	N	Y	Y	N	N	Y	N	Y	N	15	N	N	N	E	N	N	N	N	TS	IJV	A	N	N	N	N	N	N	R
39	ISMAIL	56		8612/12	Y	Y	Y	Y	N	Y	N	Y	S	15	N	N	N	N	N	N	N	N	TS	SG	A	N	N	N	Y	N	N	R
40	VENKETESH	35		7496/12	N	Y	Y	N	N	Y	Y	Y	Y	13	N	N	N	E	N	N	N	SSS	N	N	P	N	N	N	N	N	N	R
41	ABDUL KADHER	25		8672/12	N	Y	Y	Y	N	Y	N	Y	Y	11	N	N	N	E	N	N	N	SSS	N	N	P	N	N	N	N	N	N	R
42	JOHN PETER	45		5249/12	N	Y	Y	N	N	Y	Y	Y	Y	12	N	N	N	E	N	N	N	SSS	N	N	P	N	N	N	N	N	N	R
43	RAGHU	47		8945/12	N	N	Y	Y	N	Y	Y	Y	Y	13	P	N	N	N	N	N	N	SSS	N	N	P	N	N	N	N	Y	N	W
44	SANDEEP	22		9123/12	Y	Y	Y	Y	N	Y	N	Y	N	15	N	N	N	E	N	N	N	SSS	N	N	P	N	N	N	N	N	N	R
45	HARIDOSS	40		8764/12	y	y	Y	Y	N	Y	N	Y	N	15	N	N	N	N	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
46	RAMANA	45		8826/12	Y	N	Y	N	N	Y	N	Y	Y	14	N	N	N	N	N	N	N	N	N	N	A	N	CAV	N	Y	N	N	R
47	SANTHOSH	22		7927/12	Y	Y	Y	N	N	Y	Y	Y	N	14	N	N	N	N	N	N	N	SSS	N	N	P	N	N	N	N	N	N	R
48	DAKSHANAMOORTH	34		6320/11	Y	Y	Y	Y	N	Y	N	N	Y	15	N	N	N	N	N	N	N	SSS	N	SG	A	P	N	N	N	N	N	R
49	AYYAPPAN	34		3984/12	N	Y	Y	N	N	Y	N	N	N	15	N	N	N	N	N	N	N	SSS	TS	IJV	A	N	N	N	N	N	N	R
50	BASU	35		0156/11	Y	Y	Y	N	N	Y	N	N	N	15	N	N	N	E	N	N	N	SSS	TS	SG	A	N	N	N	N	N	N	R
51	GANESAN	50		6439/12	Y	Y	Y	Y	N	Y	N	Y	Y	15	N	N	N	N	N	N	N	SSS	TS	SG	A	N	N	N	N	N	N	R
52	KARUNAI VEERAN	28		0371/13	Y	Y	Y	Y	N	Y	Y	Y	Y	13	P	N	N	N	N	N	N	N	TS	SG	P	N	N	N	N	N	N	R
53	KAMALAKANNAN	23		109/13	N	Y	Y	N	N	Y	N	N	N	15	N	N	N	N	N	N	N	SSS	TS	SG	A	N	N	Y	N	N	N	R
54	MAHENDRAN	33		783//13	Y	Y	Y	N	N	Y	N	Y	N	15	N	N	N	N	N	N	N	SSS	N	N	SAH	N	N	N	N	N	N	RR
55	MARUDHAMUTHU	25		609/13	Y	Y	Y	Y	N	Y	N	N	N	15	N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
56	SOLAI	26		5794/10	Y	Y	Y	Y	N	N	N	N	N	15	N	N	N	E	N	N	E	SSS	N	N	A	N	N	N	N	N	N	R
57	MAHESH	22		298/12	Y	Y	Y	Y	N	N	N	N	N	15	N	N	N	N	N	N	N	SSS	N	N	A	N	N	N	N	N	N	W
58	DAMODHARAN	45		896/12	Y	Y	Y	N	N	N	N	N	N	15	N	N	N	E	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
59	SATHISH KUMAR	28		1056/11	Y	Y	Y	N	N	N	N	N	N	15	P	N	N	N	N	N	N	SSS	N	N	A	N	N	N	N	N	N	R
60	MOHAN	34		8243/12	Y	N	Y	N	N	Y	N	N	N	15	N	N	N	E	N	N	N	N	N	N	A	N	CAV	N	N	N	N	R

Y = Present

P = Positive

N = Absent

SG = Sigmoid Sinus

IJV = Internal Jugular Vein

SAH = Subarachanoid Hemorrhage

E = Elevated

SSS = Superior Sagittal Sinus

TS = Transverse Sinus

CAV = Cavernous Sinus

HE = Hemorrhage

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Study of Cerebral Venous Thrombosis in Males

Principal Investigator : Dr.K.Aruna Devi

Designation : PG in DM(Neuro)

Department : Department of Neurology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 13.07.2011 at the Modernized Seminar Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate form the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

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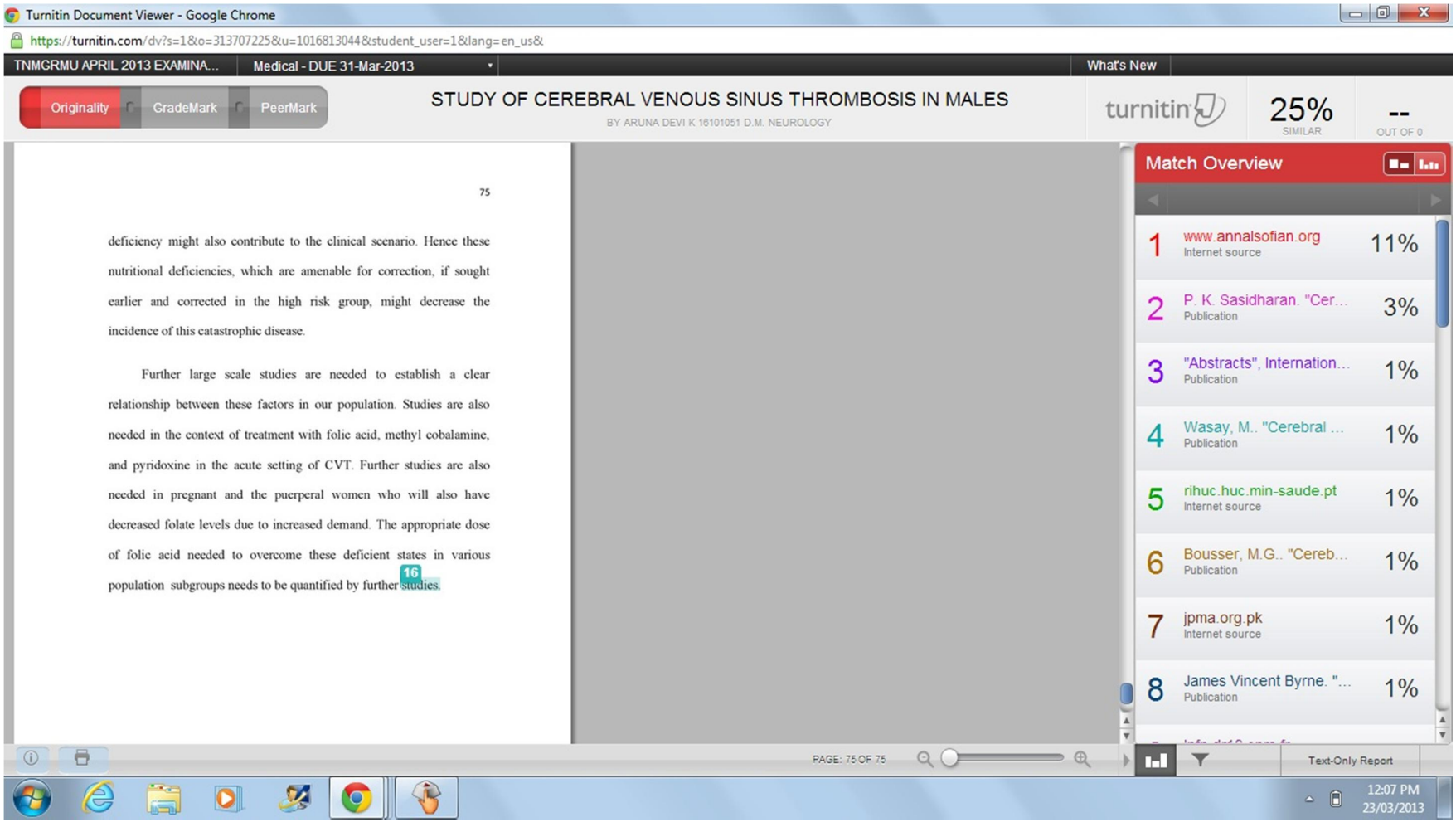
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deficiency might also contribute to the clinical scenario. Hence these nutritional deficiencies, which are amenable for correction, if sought earlier and corrected in the high risk group, might decrease the incidence of this catastrophic disease.
Further large scale studies are needed to establish a clear relationship between these factors in our population. Studies are also needed in the context of treatment with folic acid, methyl cobalamine, and pyridoxine in the acute setting of CVT. Further studies are also needed in pregnant and the puerperal women who will also have decreased folate levels due to increased demand. The appropriate dose of folic acid needed to overcome these deficient states in various population subgroups needs to be quantified by further studies.
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