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ORIGINAL ARTICLE

Clinical profile and outcome of cerebral venous sinus thrombosis at hospital discharge: a study from a tertiary care neurological center, Kathmandu, Nepal

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ABSTRACT

Introduction: To understand the clinical presentation and outcome of cerebral venous sinus thrombosis cases at discharge, we studied the clinical details and modified Rankin Scale in patients admitted and treated for cerebral venous sinus thrombosis.

Materials and methods: In this retrospective study, all the patients treated for cerebral venous sinus thrombosis who were admitted between July 2015–May 2017 A.D. were included. The clinical, laboratory and outcome details were documented. The outcome was measured in modified Rankin Scale.

Results: Out of 19 patients, most of the patients (15, 79%) were adults (19–45 years). One patient (5.2%) had obvious risk factor (post–partum state). Headache was the leading symptom in 16 (84.2%) cases and one (5.2%) had cranial nerve palsy and only three patients (15.7%) had motor deficits. Most of the patients (15, 79%) had ≥1 cerebral venous sinus involved. All the patients had modified Rankin Scale of 2 at discharge.

Conclusion: Appropriately treated cerebral venous sinus thrombosis cases, irrespective of the demographics and sinuses involved, have favourable outcome as measured by modified Rankin Scale at hospital discharge.

Keywords: Cerebral venous sinus thrombosis; CVST; Hypercoagulable states; Oral contraceptive pills; Stroke

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INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a total or partial occlusion of dural venous sinuses or the cortical veins that can cause vascular clogging leading to focal or generalized neurological deficits.[1] It is an unusual cause of cerebrovascular accident but a grave disorder especially affecting individuals in their youth.[2] The likelihood of missing the diagnosis is high because of myriad presentation mimicking other diseases.[3,4] Despite of many advances in diagnosis and management of CVST, management can still be enormously challenging because of the variety of underlying risk factors and the absence of a uniform treatment guideline which ultimately influences the outcome. Understanding the clinical profile of patients with CVST may help early diagnosis and assist in specific management and finally influences the better outcome. We therefore studied clinical profiles of patients with CVST admitted to our center and their outcome at hospital discharge.

MATERIALS AND METHODS

We performed a retrospective analysis of all patients with CVST admitted to Upendra Devkota Memorial–National Institute of Neurological and Allied Sciences (UDM–NINAS), which is a 100–bedded tertiary care neurological center situated in Kathmandu, the capital city of Nepal. All the discharge records between July 2015 and May 2017 were examined to identify the cases diagnosed to have CVST. The available clinical details, lab parameters and outcomes were meticulously recorded. The motor outcome was measured by modified Rankin Scale (mRS) which ranges from 0–6 with the lowest referring to normal motor power and highest to death (*see Annex–1*). The mRS of ≤2 was considered as a good outcome. All the patients had received the standard treatment with weight–adjusted subcutaneous low–molecular weight heparin, later substituted by warfarin and the dose adjusted to achieve target INR of 2.5–3.0, irrespective of the presence of intraparenchymal hemorrhage and other conservative treatment as per the physicians' discretion during the hospital stay. The data obtained were subjected to descriptive analysis using SPSS 20.0. Approval and ethical clearance from the institutional review board (UDM–NINAS) to conduct this study was obtained.

RESULTS

A total of 19 patients with CVST were identified. The median duration of illness was 6 days (range 1–120 days). By ethnicity, majority were Bahun. (Fig 1) The mean age was 35.6 ± 9.1 years. Most of the patients were in the age–group of 19–45 years and majority of them were males. (Fig 2 and Fig 3) Most of the patients were from Kathmandu and rest from other parts of the country (Fig 4).

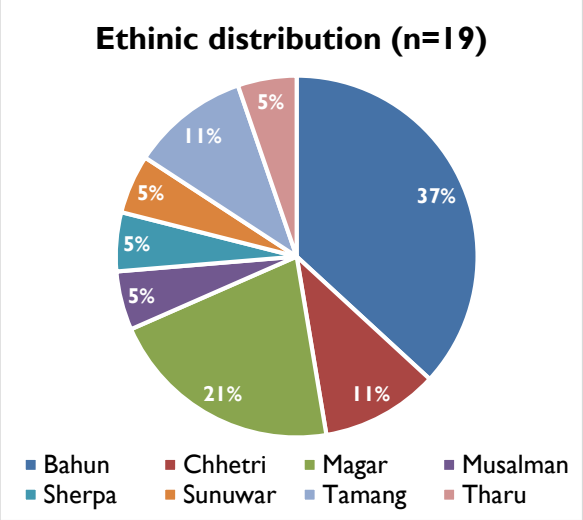

Fig 1: *Ethnic distribution of patients with CVST.*

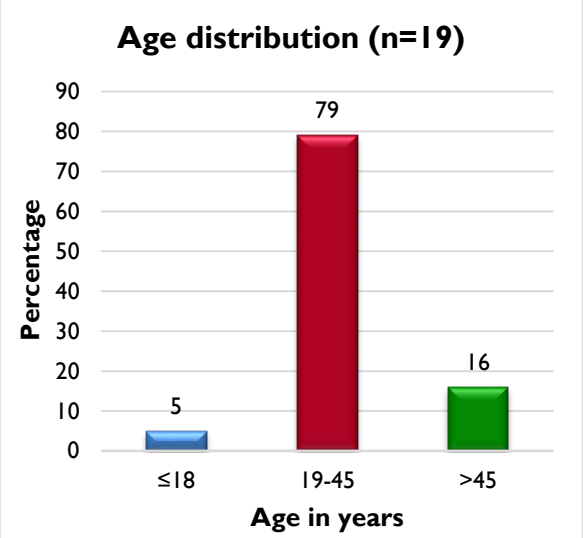

Fig 2: *Age distribution of patients with CVST.*

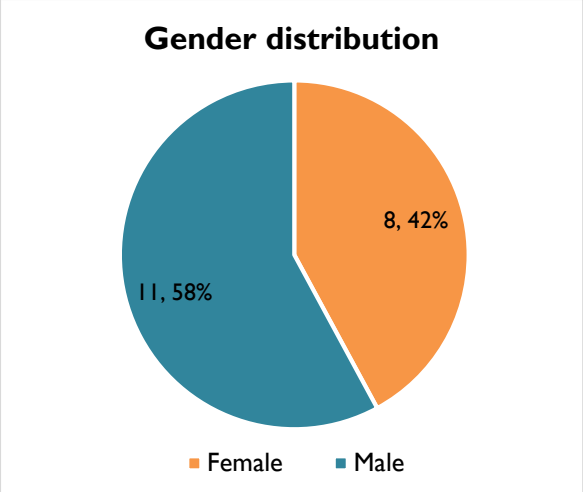

Fig 3: *Gender distribution of patients with CVST.*

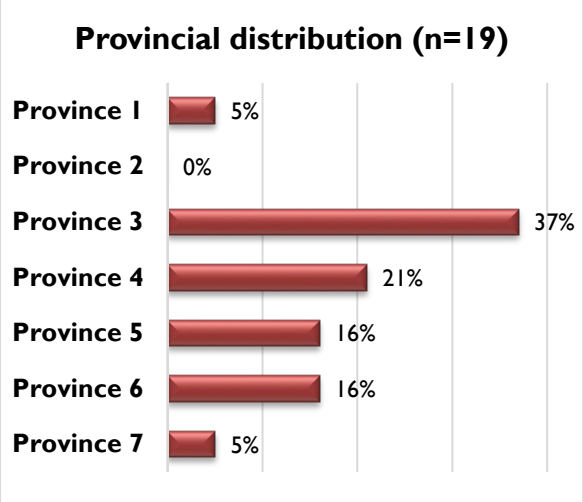

Fig 4: *Provincial distribution of patients with CVST.*

One patient was in 15th day of post–partum state. Two patients (10.5%) were smokers and three (15.8%) had history of alcohol use. None of the female patients had history of oral contraceptive pills (OCPs) use.

Headache was the leading symptom (16, 84.2%) followed by vomiting (13, 68.4%). Only one patient (5.3%) had seizure and one (5.3%) had right 6th cranial nerve palsy. One (5.3%) had vague symptom like pain in the nape of the neck (table 1).

The laboratory values are displayed in table 2.

Majority (15, 79%) had multiple dural venous sinuses involved and only four (21.1%) had single venous sinus involvement. Brain infarction was seen in five patients (26.3%), hemorrhagic infarction in two (10.5%) and intraparenchymal hemorrhage in five (26.3%). Sub–arachnoid hemorrhage was present in one patient (5.3%).

D–dimer (normal <400ng/ml) was elevated in three patients (50%) out of six available reports. Fibrin degradation products (FDP) was elevated only in one patient (16.7%) out of six patients (normal <200ng/ml).

Table 1: Clinical features of patients (n=19)

Symptoms	n (%)
Headache	16 (84.2)
Vomiting	13 (68.4)
Nausea	11 (57.9)
Seizures	1 (5.3)
Motor deficits	3 (15.8)
Visual blurring	4 (21.1)
Sixth CN palsy	3 (15.8)
Slurred speech	3 (15.8)

Abbreviations: CN, Cranial Nerve.

Table 2: Laboratory values (n=19)

Laboratory parameters (units)	n(%)
Hemoglobin (gm%)	13±5.12
Platelets (per mm^3)	191263±88948
Prothrombin time (sec)	17±11.25)
International Normalized Ratio	1.26± 0.95
Random Blood Sugar (mg%)	90.11±46.74
Urea (mg%)	22.6±10.23
Creatinine (mg%)	0.76±0.34
Sodium (mEq/L)	124.53±44.01
Potassium (mEq/L)	3.62±1.36
SGOT (U/L)	23.79±17.11
SGPT (U/L)	27.74±21.32
ALP (U/L)	66.58±35.43
D-dimer (ng/mL)	251.42±638.7
FDP >200 (ng/mL)	[a]1
FDP <200 (ng/mL)	[a]5

Notes: [a]Number of patients. Data available for only six patients.
Abbreviations: SGOT, Serum Glutamic Oxaloacetic Transaminase; SGPT, Serum Glutamic Pyruvic Transaminase; ALP, Alkaline Phosphatase; FDP: Fibrin Degradation Products.

DISCUSSION

CVST is a uncommon,[5] yet important, causes of stroke accounting almost 0.5% of all strokes.[2] In an unpublished data, over a period of one year (2071 BS) almost 25% of all the hospital admissions was of stroke and CVST constituted about 2% of all stroke. Patients may report late to the hospital, like one in our case who presented at almost four months because of the indistinct symptomatology like headache, nausea and vomiting which at times may be mild. Ethnic

prevalence of this disease is largely unknown in Nepal. Ascertainment of the ethnic incidence may provide insight into the disease pathogenesis. CVST unlike stroke affects younger individuals commonly.[2] This disease, hence is of importance not only to the family but to the society and country. Our study showed that majority of the patients were from Kathmandu. This might be possible due to patients providing their temporary address in Kathmandu while they visit hospitals like UDM–NINAS which receives cases from all over Nepal. Therefore, the high number of CVST cases cannot be clearly interpreted as a true prevalence of Kathmandu but rather could be considered as a representative hospital based prevalence of Nepal.

Number of risk factors are incriminated to CVST. In about 80% of cases, predisposing factors can be recognized.[6] Common causes are oral contraceptive pills,[7] malignancies,[8] hypercoagulable and inflammatory disorders,[6] infections,[8] dehydration[9] and head injury.[10] In the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) registry, 44% of the patients had one risk factor.[11] In our cases only one lady was in her 15th day post–partum state. Post–partum state is a hypercoagulable state due to enhanced platelets adhesion and increased coagulation factors and can cause CVST.[12,13,14] Smoking and alcohol use was found in few of our patients. Their association with CVST is uncertain, albeit alcohol causing CVST has been reported.[15,16] Activation of the clotting cascade, dehydration and resultant hyperviscosity due to alcohol have been proposed.[17,18,19] Smoking causing CVST as a result of polycythemia is also reported.[20] However, none of our patients, either smoker or non–smoker, had polycythemia. Interestingly, none of our female patients were on OCPs. OCPs usage is significantly associated with CVST.[7] it is to be noted that underlying etiology or risk factor for CVST is found in approximately 13% of adult patients. Increased number of elder patients (about 37%) do not have identifiable risk factors than in adults.[21]

There are myriad symptoms of CVST.[22,23] Common symptoms include severe headache,[24] visual disturbances,[25] fainting or loss of consciousness, motor weakness,[26] and seizures.[27] Headache is known as the most common symptom.[11,28,29] Our cases had headache as the commonest symptom. Increased intracranial pressure, subarachnoid hemorrhage, stretching of nerves in sinus walls, and sinus inflammation may be responsible for headache. Seizure can manifest in CVST because of the ischemia to neurons or bleed into the parenchyma. Pain at the nape of the neck may be of interest. Raised intracranial pressure and sigmoid sinus involvement can potentially cause neck pain. About 3–5% of CVST can have subarachnoid hemorrhage.[30] The exact mechanism is unknown, however rupture of venous parenchymal hemorrhage into subarachnoid space,[31] venous hypertension leading to vessel rupture and blood seepage into the subarachnoid space,[32] and local inflammatory response and endothelial dysfunction causing increased vascular permeability leading to blood extravasation into subarachnoid space have been postulated.[33]

Nearly 15% of our patients had motor weakness. About half of the patients with CVST develop cerebral parenchymal lesions and neurological signs.[26] Multiple venous sinus thrombosis was an interesting finding in our study. Multiple venous sinuses are involved in almost 50–60% of cases.

Superior sagittal sinus was common sinus involved. The preference of superior sagittal sinus is because of the size, location, flow dynamics and the pattern of drainage.[34] The next common sinus was transverse sinus. The main cerebral venous sinuses affected by CVST are the superior sagittal sinus (72%) and the lateral sinuses (70%). In about one–third of cases more than one sinus is affected.[35] The ISCVT determined the frequency of the sites of CVST as follows: Transverse sinus 86%, superior sagittal sinus 62%, straight sinus 18%, cortical veins 17%, jugular veins 12%, vein of Galen and internal brain veins 11%.[11]

The neuroimaging features of CVST can include focal areas of edema or venous infarction, hemorrhagic venous infarction, diffuse brain edema, or (rarely) isolated subarachnoid hemorrhage.[36] Radiologically, hemorrhagic infarction affronting the arterial boundary is a classical finding in CVST. Majority of our patients

had only hemorrhage or ischemia. Few had hemorrhagic infarct. However, we had not used gradient echo sequence in Magnetic Resonance Imaging which could have detected higher bleeding into the infarcted area. In patients with CVST, the proportion who present with intracerebral hemorrhage is 30 to 40 percent.[28,37] Small nontraumatic juxtacortical hemorrhages, which are located just below the cortex in the white matter and have a diameter of <2 cm, account for up to one–half of intracerebral hemorrhages in patients with CVST and are associated with superior sagittal sinus occlusion.[38]

Of the available data, D–dimer and FDP were raised in limited patients. In CVST patients, raised FDP is found in patients with raised D–dimer.[39] However, a normal D–dimer value does not rule out CVST in a patient with risk factors. Although in acute phase (≤7 days), the sensitivity and specificity of D–dimer in diagnosis of CVST may be higher (94 and 99%),[40] in general the specificity can go low up to 94%.[41] Unlike, deep vein thrombosis of lower limbs, role of D–dimer in CVST is controversial because it is elevated in neurodeficient CVST but low in CVST with isolated headache.[42]

The overall outcome of treated CVST is good as compared to other types of stroke. Similar was our finding. There was no death and all the patients were discharged with favorable outcome of mRS of 2. The long term outcome has been observed at our institution and was favorable. Between 57–86% of patients have complete recovery and mortality ranges between 5.5% and 18%.[43,44] it is to be noted that there is no clear correlation between disease severity and outcome.[8,45]

Our study has few limitations. As this is a retrospective study, few important data pertaining to the study were missing. There was no accurate documentation of admission disability, however we aimed to examine the overall outcome of treated patients irrespective of their disability at admission. Also, we did not have in–depth study of thrombophilia and malignancy screening. A large sample size would have been definitely superior but we intended to study cases presenting to us over a defined period only.

CONCLUSION

Appropriately treated CVST cases, irrespective of the sinuses involved, have favorable outcome as measured by mRS at hospital discharge. A large prospective trial to explore the early outcome of CVST patients receiving treatment is recommended.

COMPETING INTEREST

The authors declare that there are no competing interests regarding the publication of this paper.

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Annex–1: Modified Rankin Scale

Score	Description
0	No symptoms at all.
1	No significant disability despite symptoms; able to carry out all usual duties and activities.
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.
3	Moderate disability; requiring some help, but able to walk without assistance.
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention.

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