

Research Paper:

The Clinical Profile and 1-year Prognosis of Patients With Cerebral Venous Sinus Thrombosis: A Study in Qom Province, Iran



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ABSTRACT

Background and Aim: Cerebral Venous Sinus Thrombosis (CVST) is a rare cerebrovascular accident with a variety of clinical symptoms. As there is evidence of a higher rate of CVST in Iran, we aimed to investigate the frequency of CVST, its predisposing factors, and 1-year prognosis in Qom Province, Iran.

Materials and Methods: We performed a cross-sectional study from 2018 to 2020 in Beheshti Hospital, Qom City, Iran. We reviewed the clinical and para-clinical records of the patients by a checklist. Follow-up visits were performed at 12 months to evaluate the CVST recurrence, the neurological status according to modified Ranking Score (mRS), and persistence of neurological complaints. Eventually, we used SPSS version 22 to analyze the obtained data.

Results: We identified 57 cases of definite CVST, which accounted for 2.5% of all cerebrovascular accidents in this period. We revealed a higher incidence of CVST among the women (68.4%). The use of oral contraceptives, pregnancy, and postpartum status were considered the main risk factors (n=32/39). We also revealed evidence of inherited coagulopathy in 14.03% of our patients, mainly due to protein S deficiency (n=5). The superior sagittal sinus was the main involved sinus (68.42%) associated with other sinus thromboses in 22% of all cases. We also showed a significant short-term and long-term recovery of the disease with a mean mRS score of 1.22 at discharge and 1.12 at a 1-year follow-up.

Conclusion: Oral contraceptives and fasting could contribute to developing CVST. We also revealed a favorable outcome following urgent treatment.

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1. Introduction

Cerebral Venous Sinus Thrombosis (CVST) is a relatively rare disorder of the cerebral venous system accounting for less than 1% of all strokes [1]. The clinical manifestation has a remarkable wide spectrum from mild headache and other signs of raised intracranial pressure to seizure, focal neurological deficit, altered consciousness, and even death [2]. The annual incidence of Cerebral Venous Thrombosis (CVT) is estimated to be 1 per 100000, which mainly affects women of childbearing age. Notably, there is evidence of a higher incidence in Iran compared to European countries, which might be attributed to the differences in the risk factor profile of Iranian patients. The use of oral contraceptives is more common among Muslim women during religious ceremonies as fasting in Ramadan, which contributes to venous thrombosis formation [3, 4]. The various clinical presentations associated with CVST makes it a diagnostic challenge that might lead to permanent disability or even mortality in cases of misdiagnosis.

Regarding the limited data on the prevalence of CVST in Iran, we aimed to investigate the frequency of CVST among all cases of cerebrovascular accidents in Qom Province as the most religious province in Iran to provide comprehensive knowledge toward the clinical management of the disease.

2. Materials and Methods

Study design

This cross-sectional study was conducted in Qom Province, Iran, from 2018 to 2020. The study was approved by the local Ethics Committee (Ethical code: IR.MUQ.REC.1398.155). In addition, written informed consent was obtained from all patients before they participated in this study.

Study population

We enrolled all patients admitted to Beheshti Hospital, Qom City, Iran with a diagnosis of CVST. Patients younger than 18 years old, patients of the cerebrovascular accident other than CVST as arterial stroke or lobar intracranial hemorrhage associated with hypertension, and patients who lost the follow-up were excluded. The diagnosis of CVST was made based on clinical symptoms, neurological examinations, and neuroimaging studies.

Intervention and data gathering

The data collection was prospectively performed by a checklist consisting of clinical profile, neuroimaging results, para-clinical measures, modified Ranking Score (mRS) at discharge, and 1-year prognosis.

The clinical profile included demographic features as age, sex, Body Mass Index (BMI), past medical history, habitual file, current medication usage, pregnancy, recent fasting, familial history, physical and neurological complaints, the onset of symptoms, and the clinical symptoms according to the National Institutes of Health Stroke Scale (NIHSS) score. Neuroimaging included brain Computed Tomography (CT), brain Magnetic Resonance Imaging (MRI) with and without gadolinium, and brain MR venography. The laboratory profile included routine blood chemistry, complete blood count, Erythrocyte Sedimentation Rate (ESR), Prothrombin Time (PT), Partial Thromboplastin Time (PTT), International Normalized Ratio (INR), anti-thrombin III, protein C and protein S, C3, C4, Anti-Nuclear Antibody (ANA), anti-cardiolipin antibody, lupus anticoagulant, anti-double stranded DNA (anti-dsDNA).

Follow-up visits were performed at 12 months by direct interview and observation. Follow-up data were disability score according to mRS, 12 death, recurrence of CVST, new thrombotic events, the persistence of neurological complaints as seizures, headache, blurred vision and diplopia, pregnancy, abortion, and current treatment.

Statistical analysis

Eventually, we used SPSS version 22 (SPSS Inc., Chicago, IL, USA) to analyze the obtained data. The results are presented as Mean \pm SD for continuous or frequencies for categorical variables. The Chi-square and independent t tests were used for comparison between quantitative and qualitative variables. A P value less than 0.05 was considered significant.

3. Results

During the three-year study period, 57 patients were identified with a definite diagnosis of CVST. Notably, the total admission of cerebrovascular accidents was estimated to be 2270 during this period. The Mean \pm SD age of participants was 39.96 \pm 12.22 years. The majority of patients (68.4%) were female.

Of them, two (5.12%) were pregnant and 10 (17.54%) postpartum. Twenty women of reproductive age were

also taking oral contraceptives (51.28%). No postmenopausal women were on hormone replacement therapy at the time of thrombosis. Two patients were pregnant (5.21%), and 10 patients (17.54%) were postpartum. One patient reported a history of spontaneous abortion. Other risk factors were dehydration associated with fasting in 20 patients (38.6%) and a history of recent sinusitis in 8 patients (14%). Of the 20 patients with a history of Oral Contraceptive (OCP) consumption, 10 patients took the medication during Ramadan.

The summary of patients' characteristics is presented in Table 1. Based on our results, all patients had some degree of headache. Three patients (5.55%) presented with thunderclap headaches, one of which was complicated with focal seizure and left hemiparesis on admission. Other manifestations were hemiparesis (5 patients, 8.77%), new-onset seizure (4 patients, 7.01%), diplopia (4 patients, 7.01%) and acute confusional state (2 patients, 3.50%).

In terms of radiologic features, evidence of hemorrhage was seen in 12 patients (21.05%). Acute thrombosis in the involved sinuses (cord sign) was evident in six subjects (10.52%). Venous infarction occurred in 9 patients (15.78%), including one case (2%) with bilateral thalamic infarct and eight cases (14.03%) with hemorrhagic infarction, which was accompanied by significant edema and midline shift in one case. We also found evidence of thin cortical subarachnoid hemorrhage in two cases (3.50%). Partial or complete occlusion of the superior sagittal sinus was observed in 68.42% of cases (n=39). It was mainly associated with concomitant occlusion of other sinuses (18 patients with transverse sinus thrombosis, 3 patients with transverse sinus and jugular vein thrombosis, and one with deep cerebral vein thrombosis). In the remaining 17 patients, isolated involvement of superior sagittal sinus was evident. The radiologic characteristics of our patients are summarized in Table 2.

Furthermore, we found the evidence of inherited deficiency of coagulation factors in 7 patients (12.4%), which was mainly protein S deficiency (n=5). Additionally, 1 patient was diagnosed with antiphospholipid antibody syndrome due to clinical history and high titer of lupus anticoagulant antibody, ANA, and ds-DNA.

In terms of clinical management, we recorded the medical profile of our patients. All patients were initially treated with IV anticoagulants such as unfractionated heparin or low-molecular-weight heparin except in four cases with Massive Intracranial Hemorrhage (ICH). In this subgroup, the anticoagulant started with a delay of 48 hours. However, one patient underwent hemi-craniotomy,

and anticoagulant therapy was postponed due to serious clinical and neuroimaging status. Anticonvulsants were prescribed only in patients with cortical infarction (n=8), clinical seizure (n=4), and decreased level of consciousness (n=2). Based on the clinical situation, patients were eventually started with warfarin with INR maintained between 2 to 3 for 6-12 months.

Except for the patient who underwent hemicraniotomy, all patients improved significantly regardless of the severity of symptoms. The mean mRS at discharge was estimated to be 1.22. The 1-year follow-up revealed a complete recovery in 27 patients (47.36%) with a mean mRS score of 1.10 (except the one who died and the one with significant focal neurological deficit, the rest of the patients had an mRS score of 1). However, 14 patients (24.56%) still had occasional headaches. While no patient had a history of recurrent seizures, two patients remained on anticonvulsant therapy. Notably, one patient discontinued his medication resulting in the symptoms of flare-up and readmission.

4. Discussion

The incidence of CVST is not well-studied. In our study, we revealed that CVST accounts for 2.5 % of all cerebrovascular accidents, which is higher than other countries. In line with previous reports in Iran [5-9], we revealed that most of our patients were female (68.42%), and the main predisposing factors of CVST were oral contraceptive consumptions and the dehydration associated with fasting. Given that most Iranians are Muslim, there is a strong tendency among women to use oral contraceptives to perform their religious duties in Ramadan, often without consulting a physician. Moreover, prolonged dehydration might increase the chance of thrombosis formation in association with oral contraceptive consumptions. There is also evidence of non-Iranian reports focusing on the association of oral contraceptive and CVST. For example, Vembu P et al. highlighted the role of oral contraceptive on CVST development in a case series of 72 patients [10]. As there is increasing evidence of cerebrovascular accidents in females in either form of acute ischemic stroke with a preference in premenopausal period or venous involvement as CVST in reproductive age, more attention should be paid toward modifying risk factors like oral contraceptive among the women to prevent from the cerebrovascular accidents accounting for the most cause of morbidity worldwide [11, 12].

On the other hand, the clinical manifestation of our patients was consistent with other reports as all patients had some degree of headache in association with the focal

Table 1. The baseline characteristics of the patients with cerebral venous sinus thrombosis

Characteristics		Patients, No. (%)
Gender	Female	39 (68.4)
	Male	18 (33.6)
Oral contraceptive consumption		20 (51.28% of female were in reproductive age)
Pregnancy or postpartum status		12 (21.05)
History of spontaneous abortion		1 (1.75)
Fasting (dehydration)		20 (38.6)
Recent sinusitis		8 (14)
Recent head trauma		4 (7)
History of coagulopathy as deep vein thrombosis		0 (0)
Past-medical history		29 (50.9)

neurological deficit (8.77%), seizure (7.01%), diplopia (7.01%), and acute confusional state (3.50%). Similarly, we found that the superior sagittal sinus was the most involved sinus (68.42%).

In terms of prognosis, we observed a considerable recovery. Except for the one who died because of massive hemorrhage and vasogenic edema and the one with 1-year mRS of 3, all patients had a favorable outcome with a mean mRS of 1.22 and complete recovery of symptoms of 47.36%. Our results revealed a better re-

Table 2. The radiologic features of the patients with cerebral venous sinus thrombosis

Neuroimaging Modality		Patients, No. (%)
Brain CT	Acute thrombosis in sinus	6 (10.52)
	Hemorrhagic infarct	8 (14.03)
	Isolated ischemic infarct	0 (0)
	Subarachnoid hemorrhage	2 (3.50)
Brain MRI	Hemorrhagic infarct	8 (14.03)
	Isolated ischemic infarct (bilateral thalamic infarct)	1 (1.75)
	Subarachnoid hemorrhage	2 (3.50)
Brain MRV	Superior sagittal sinus	39 (68.42)
	Transverse sinus	21 (36.48)*
	Cortical vein	8 (14.03)
	Deep cerebral vein	1 (1.75)*
	Jugular vein	3 (5.26)*

*All cases of transverse sinus thrombosis, jugular vein thrombosis, and deep cerebral vein thrombosis were accompanied with superior sagittal sinus thrombosis; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; MRV: MR Venography.

covery compared to previous reports. About 21% of patients in the study of Vembu P et al. required intensive care unit with ventilator support [10]. In another report, a favorable outcome of 83% was observed as 6 patients were dependent on a long-term follow-up [13]. Additionally, in a prospective multicenter international study of 624 CVST patients, 8% of the patients died, either as a direct consequence of CVT or due to an underlying condition. Based on their results, the poor prognostic factors included male sex, age >37 years, coma, mental status disorder, intracranial hemorrhage on admission, thrombosis of the deep cerebral venous system, central nervous system infection, and cancer. However, as only one of our patients died due to CVST, we could not conclude the underlying risk factors.

Regarding the cultural and religious issues, CVST is more common in Iran than other countries. One of our study's strong points was the evaluation of CVST prognosis, as the majority of the reports in Iran are confined to the risk factors of CVST. However, we followed patients for only one year, and we used mRS and patients' history of neurological complaints as an outcome assessment tool. However, despite a favorable outcome, long-term follow-up studies suggest a high prevalence of ongoing neuropsychiatric complaints, with one-quarter of them unable to return to work [14]. We recommend more comprehensive studies focusing on the long-term outcome of patients with CVST considering all aspects of neuro-cognition.

5. Conclusion

Our results highlighted the higher incidence of CVST in Qom Province, Iran affecting mainly women with a history of using oral contraceptive and fasting. We also emphasized the early diagnosis of CVST, which contributes to a significant recovery.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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