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Clinical features, common characteristics, and outcomes of cerebral venous sinus thrombosis in Northwest Iran: A retrospective descriptive cohort study

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Keywords
Cerebral Venous Sinus Thrombosis; Stroke; Characteristics; Outcomes; Iran

Abstract

Background: Cerebral venous sinus thrombosis (CVST) is an uncommon but increasingly recognized cause of stroke. Despite a higher prevalence in developing regions, comprehensive data from these areas remain scarce. This study aims to describe the clinical features, common exposures, and outcomes of patients with CVST in Northwest Iran.

Methods: A retrospective descriptive study was conducted between September 2018 and September 2020 in Tabriz City, Iran. Data on demographics, common characteristics, clinical presentations, imaging findings, and outcomes were collected from Tabriz Stroke Registry. The modified Rankin Scale (mRS) was used to assess outcomes at 1, 6, and 12 months. Statistical analysis was performed, employing descriptive statistics and normality tests.

Results: A total of 128 patients were included, predominantly women (76.6%) with a median age of 36.5 years. Common characteristics included contraceptive use (37.5%), infections (5.5%), and fasting (9.4%). Headache was the most frequent symptom (91.7%), followed by papilledema (53.3%) and seizures (43.3%). At one month, 86.7% of patients achieved a favorable outcome (mRS < 3), with mortality rates of 2.5%, 3.7%, and 4.5% at one, six, and twelve months, respectively.

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Imaging data indicated that the transverse/sigmoid sinuses (66.7%) and superior sagittal sinus (62.2%) were the most commonly affected.

Conclusion: Among hospitalized patients with stroke in our tertiary centers, the proportion of CVST appears higher than those reported in many Western hospital-based series. Headache was the most common presentation; oral contraceptive use and fasting were frequently observed exposures. Population-based and controlled studies are needed to estimate true incidence and evaluate causal risk factors.

Introduction

Cerebral venous sinus thrombosis (CVST) is a relatively rare form of stroke, with an estimated incidence ranging from 2.45 to 3.16 cases per 100000 population.[1,2] The increasing awareness of CVST and advancements in neuroimaging modalities have led to a higher detection rate in recent years.[3] CVST accounts for only 0.5%-1% of all strokes, predominantly affecting young women in their third decade of life.[4] Several risk factors have been associated with the development of CVST, including genetic predispositions, thrombophilia, malignancies, infections, surgery, trauma, hormonal changes such as those induced by contraceptive pills, pregnancy, and postpartum periods.[5-11]

In developing countries like Iran, Pakistan, and India, the reported prevalence of CVST is higher than that in Western countries.[12-14] For example, Iran has a prevalence of approximately 12.3 cases per million population, with mortality rates also exceeding those reported in Western cohorts.[15,16] Despite the rising prevalence of CVST, there is limited literature regarding its epidemiology, clinical features, radiological manifestations, treatment options, and prognosis, particularly in the Eastern Mediterranean region. The present study aims to address this gap by investigating the clinical features, common exposures, and outcomes of patients with CVST in Northwest Iran.

Materials and Methods

This retrospective descriptive study was conducted at Imam Reza and Razi Referral Hospitals, affiliated with Tabriz University of Medical Sciences, Tabriz, Iran, between September 2018 and September 2020. The study protocol was approved by the Ethics Committee of School of Medicine, Tabriz University of Medical Sciences (ethics code: IR.TBZMED.REC.1398.671).

Inclusion criteria comprised all consecutive patients with a confirmed diagnosis of CVST and complete available demographic and clinical data. Exclusion criteria were incomplete records or uncertain CVST diagnosis. Diagnosis was confirmed by a neurologist based on clinical presentation and neuroimaging evidence, utilizing either magnetic resonance (MR) venography or computed tomography (CT) venography.

The study cohort included all eligible consecutive patients during the study period; therefore, no a priori sample size calculation was performed. Data on demographics, clinical presentation, common characteristics, imaging findings, and outcomes were extracted from Tabriz Stroke Registry.[17] Since data were retrieved retrospectively from Tabriz Stroke Registry, independent informed consent was not obtained from the patients at the time of conducting the study. However, consent was obtained from the participants at the time of hospitalization. In this registry, data on exposures such as contraceptive use, fasting, and infections were obtained from patient self-report at admission and documented in the medical records. Fasting was defined as self-reported voluntary abstinence from food and drink for ≥ 12 consecutive hours within the 7 days prior to symptom onset. Infections included physician-diagnosed acute bacterial or viral infections that were clinically active at the time of admission. Diagnoses were based on history, physical examination, and/or relevant laboratory or imaging findings, as documented in the medical records. Exposure variables such as contraceptive use and pregnancy status were obtained from patient or family self-report at admission and verified when possible from medical records.

The modified Rankin Scale (mRS) was employed to assess patient disability at one, six, and twelve months post-diagnosis. Follow-up assessments at 1, 6, and 12 months were conducted during scheduled neurology clinic visits; when in-person evaluation was not possible, data were obtained via structured telephone interview.

For each variable, analyses were conducted on a complete-case basis, meaning that only participants with available data for that variable were included in its analysis. As a result, denominators may vary across variables and are indicated in the corresponding tables, footnotes, or figure captions. No statistical imputation for missing data was performed.

Descriptive statistics were used to summarize the data, including percentages, means, standard

deviations (SDs), medians, and interquartile ranges (IQRs), depending on the distribution of variables, which was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. However, no hypothesis tests were performed to infer associations. All percentages include denominators and 95% confidence intervals (CIs). Statistical analyses were performed using SPSS software (version 25, IBM Corporation, Armonk, NY, USA).

Results

Overall, 128 CVST cases were included in this study. Detailed patient characteristics, including history of CVST, pregnancy, trauma, fasting, hospital stay duration, malignancies, infections, contraceptive use, and recurrence of thromboembolic events, are presented in table 1. Symptoms were available for 120 of the 128 patients (Table 2), as 8 patients had incomplete documentation of presenting symptoms. Outcomes were assessed in those successfully followed at each time point (Table 3). All 120 patients completed the 1-month follow-up, with no missing data at this stage.

Table 1. Characteristics of the patients with cerebral venous sinus thrombosis (CVST)

Characteristic		n (%)	95% CI
Sex	Men	30 (23.4)	16.9-31.5
	Women	98 (76.6)	68.5-83.1
History of CVST		2 (1.6)	0.4-5.5
Familial history for CVST		1 (0.8)	0.1-4.3
Pregnancy*		4 (4.1)	1.6-10.0
Trauma		4 (3.1)	1.2-7.8
Fasting		12 (9.4)	5.4-15.7
Malignancies	Total	4 (3.1)	1.2-7.8
	Ovarian	1 (0.8)	0.1-4.3
	Lymphoma	1 (0.8)	0.1-4.3
	Breast	1 (0.8)	0.1-4.3
	Colorectal	1 (0.8)	0.1-4.3
Infections	Total	7 (5.5)	2.7-10.9
	Sinusitis	1 (0.8)	0.1-4.3
	Mastoiditis	1 (0.8)	0.1-4.3
	Meningitis	1 (0.8)	0.1-4.3
	Brucellosis	1 (0.8)	0.1-4.3
	Others	3 (2.3)	0.8-6.7
Contraceptives*	Total	48 (49.0)	39.3-58.7
	LD	37 (37.8)	28.8-47.6
	Cyproterone compound	3 (3.1)	1.0-8.6
	Progesterone ampoule	2 (2.0)	0.6-7.1
	DMPA	1 (1.0)	0.2-5.6
	Drospirenone	1 (1.0)	0.2-5.6
	Lynestrenol	1 (1.0)	0.2-5.6
	Megestrol	1 (1.0)	0.2-5.6
	Medroxyprogesterone	1 (1.0)	0.2-5.6
	Rokin and spironolactone	1 (1.0)	0.2-5.6
Medical conditions	Total	10 (7.8)	4.3-13.8
	IBD	2 (1.6)	0.4-5.5
	Polycythemia	1 (0.8)	0.1-4.3
	SLE	2 (1.6)	0.4-5.5
	Endodontics procedure	1 (0.8)	0.1-4.3
	Rheumatoid arthritis	1 (0.8)	0.1-4.3
	Klinefelter syndrome	2 (1.6)	0.4-5.5
	Homocystinuria	1 (0.8)	0.1-4.3
Thromboembolic events recurrence	Total	2 (1.6)	0.4-5.5
	Massive PTE	1 (0.8)	0.1-4.3
	DVT	1 (0.8)	0.1-4.3

Percentages are calculated from the total cohort (n = 128). No missing data were observed for the characteristics presented in this table. *Contraceptive use and pregnancy percentage are only reported among women (n = 98), as only women use oral contraceptive pills (OCPs)/get pregnant.
CVST: Cerebral venous sinus thrombosis; LD: Low dose; DMPA: Depot medroxyprogesterone acetate; IBD: Inflammatory bowel disease; SLE: Systemic lupus erythematosus; PTE: Pulmonary thromboembolism; DVT: Deep vein thrombosis; CI: Confidence interval

Table 2. The symptoms of the patients with cerebral venous sinus thrombosis (CVST)

Symptom	n (%)	95% CI
Headache	110 (91.6)	85.3-95.4
Headache type		
Diffuse	58 (48.3)	39.6-57.2
Localized	46 (38.3)	30.1-47.3
Neck pain	5 (4.1)	1.8-9.4
Others	1 (0.8)	0.1-4.6
Headache location		
Frontal	22 (18.3)	12.4-26.2
Temporal	19 (15.8)	10.4-23.4
Occipital	15 (12.5)	7.7-19.6
Periorbital	2 (1.6)	0.5-5.9
Neck	2 (1.6)	0.5-5.9
Diffuse	50 (41.6)	33.2-50.6
Photophobia	34 (28.3)	21.0-37.0
Nausea/vomiting	32 (26.6)	19.6-35.2
Seizure	52 (43.3)	34.8-52.3
Partial seizure	12 (10.0)	5.8-16.7
Generalized seizure	32 (26.6)	19.6-35.2
Status epilepticus	5 (4.1)	1.8-9.4
Unknown seizure type	3 (2.5)	0.9-7.1
Motor weakness	43 (35.8)	27.8-44.7
Papilledema	64 (53.3)	44.4-62.0

Percentages are calculated from the number of patients with available data for each symptom (n = 120).
CI: Confidence interval

At the 6-month follow-up, 13 patients were lost, including 10 who could not be contacted and 3 who had died following the previous follow-up, resulting in 107 patients included at this time point. By the 12-month follow-up, an additional 19 patients were excluded due to being unable to be contacted (n = 15) or due to death in the previous follow-up (n = 4), leaving 88 patients with available data at the final follow-up.

Imaging data on venous involvement were complete for 45 most recent patients and the older imaging data were not saved in the system (Table 4). Flow diagram of the number of patients in each step is illustrated in figure 1.

Among the 128 patients with CVST, the majority were women (76.6%), with a median age of 36.5 years. Contraceptive use was common, with 37.5% of female patients using contraceptives, particularly low-dose formulations (28.9%). Infections were present in 5.5% of cases, with 3.1% having malignancies and 7.8% having other medical conditions such as inflammatory bowel disease (IBD) (1.6%) and systemic lupus erythematosus (SLE) (1.6%). Fasting was reported by 9.4% of patients, and thromboembolic events recurrence occurred in 1.6% of cases.

Table 3. The outcomes of cerebral venous sinus thrombosis (CVST) in the patients

Outcome		n (%)	95% CI
1 month	Favorable	104 (86.6)	79.4-91.6
	Poor	16 (13.3)	8.4-20.6
	Mortality	3 (2.5)	0.9-7.1
6 months	Favorable	100 (93.4)	87.1-96.8
	Poor	7 (6.5)	3.2-12.9
	Mortality	4 (3.7)	1.5-9.2
12 months	Favorable	81 (92.0)	84.5-96.1
	Poor	7 (7.9)	3.9-15.5
	Mortality	4 (4.5)	1.8-11.1

Percentages at each time point are calculated from the number of patients successfully followed at that stage (n = 120 at 1 month, n = 107 at 6 months, n = 88 at 12 months). Losses to follow-up were due to inability to contact or patient refusal [favorable outcome: modified Ranking Scale (mRS) < 3; poor outcome: mRS ≥ 3].
CI: Confidence interval

The most common symptom in patients with CVST was headache, reported in 91.7% of cases, with diffuse headache being the most frequent type (48.3%). Papilledema occurred in 53.3% and seizures in 43.3%, predominantly generalized (26.7%). Motor weakness was noted in 35.8% of patients, while photophobia and nausea/vomiting were less common, occurring in 28.4% and 26.7% of cases, respectively. The symptom details are outlined in table 2.

At 1 month, 86.7% of patients had a favorable outcome (mRS < 3), with a mortality rate of 2.5%. At 6 months, the favorable outcome rate improved to 93.5%, with mortality at 3.7%. By 12 months, 92.0% had a favorable outcome, and mortality reached 4.54% (Table 3).

Table 4. Affected veins and sinuses

Affected vein	n (%)	95% CI	Male/female ratio
Cortical vein	5 (11.1)	4.8-23.5	2/3
Transverse/sigmoid sinus	30 (66.7)	52.1-78.6	6/24
Straight deep vein	7 (15.6)	7.7-28.8	0/7
Cavernous sinus	0 (0)	0.0-7.9	-
Superior sagittal sinus	28 (62.2)	47.6-74.9	4/24

Percentages are calculated from patients with complete imaging data (n = 45). Imaging data from older records were not available due to not being saved in the system.
CI: Confidence interval

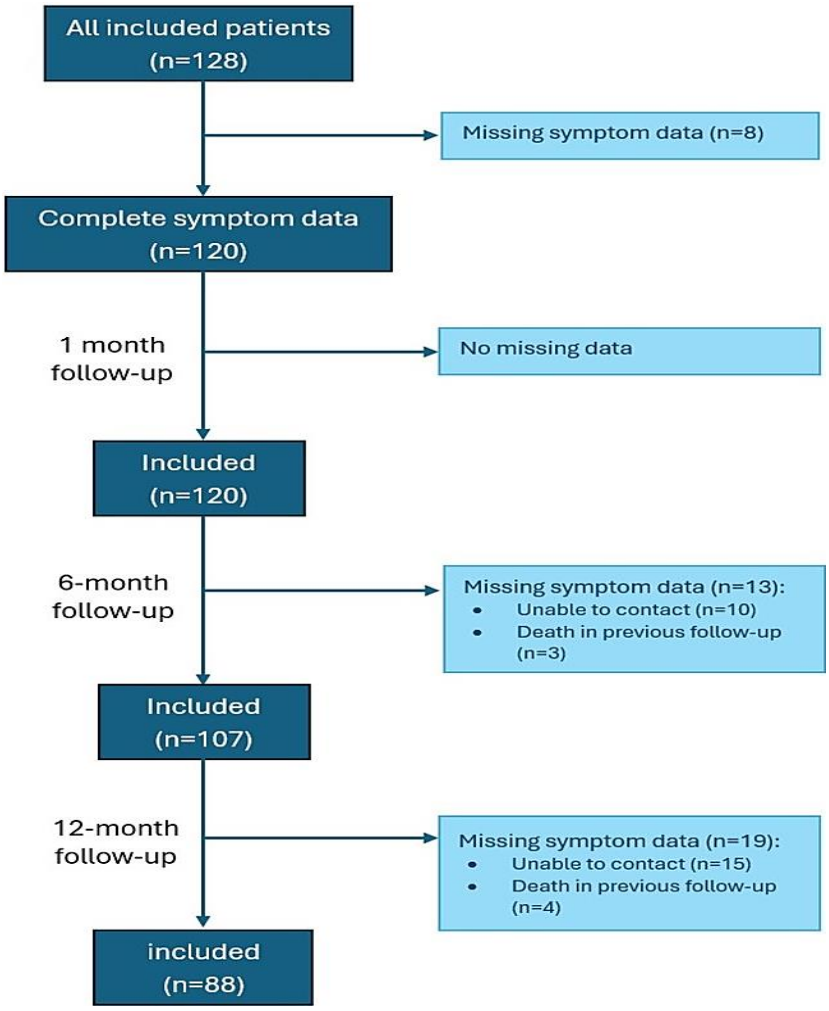

Figure 1. Flow diagram of the number of patients included in each step from the initial analyses up to the final follow-up

Only 45 most recent patients had complete imaging data. Older imaging data were not available due to not being saved in the system. The most frequently affected veins in CVST were the transverse/sigmoid sinuses (66.7%) and the superior sagittal sinus (62.2%). No cases of cavernous sinus involvement were observed (Table 4). The frequencies reported in table 4 represent the number of patients with venous involvement; these categories are not mutually exclusive, as one patient may have involvement of multiple veins.

Discussion

CVST presents a significant public health concern across various regions of Iran and Asia, characterized by diverse clinical presentations, risk factors, and mortality rates. The prevalence of CVST in Iran, and particularly in the northwestern region, appears higher than that reported in most other countries. In our center, out of approximately 1000 annual stroke admissions, around 64 cases are diagnosed as CVST – representing a much greater proportion than seen in many international studies when comparing prevalence data. We have intentionally limited such international comparisons to prevalence and clinical characteristics.

Globally, CVST accounts for only 0.5%-1% of all strokes,[18] whereas our local data highlights a substantially increased burden. This elevated prevalence may reflect regional risk factor profiles, greater clinical awareness, or differences in diagnostic practices, underscoring the importance of continued research, local surveillance, and targeted preventative strategies in this population.

This study represents a retrospective descriptive case series rather than an analytical study. In our study, headache was reported by 91.7% of patients, with diffuse headache being the

most frequent type (48.3%). This aligns with other studies from Iran and neighboring countries, where headaches were also reported as the predominant symptom. For instance, Janghorbani et al. noted that headaches were present in 83.87% of cases,[19] while a study conducted in Pakistan reported it in 97% of patients.[20] The high prevalence of headache as a symptom emphasizes the need for healthcare professionals to consider CVST in differential diagnoses when patients present with significant headaches. Recognizing this pattern can lead to earlier interventions, potentially reducing the risk of complications.

Seizures were observed in 43.3% of our cohort, with a predominance of generalized seizures (26.7%). This is consistent with findings from the northeastern region of Iran, where seizures occurred in 58% of patients.[21] The presence of papilledema in 53.3% of our patients suggests a significant burden of increased intracranial pressure, reflecting similar observations in Iranian studies.[22] The identification of seizures and papilledema as common symptoms underlines the necessity for comprehensive neurological assessments in suspected CVST cases. This awareness can improve diagnostic accuracy and facilitate timely management of this condition.

Risk factors for CVST varied across studies, but oral contraceptive pills (OCPs) emerged as a common predisposing factor. In the present study, 37.5% of female patients used contraceptives, while studies from Isfahan City, Iran, and northeastern Iran reported rates of OCP usage in patients with CVST ranging from 38.1% to 65.3%.[19,21] Notably, in northwestern Iran, the use of OCPs without medical consultation is common among young women, especially for non-therapeutic purposes such as postponing menstruation during vacations or the month of Ramadan. The recognition of OCP usage as a significant risk factor can guide clinicians in patient counseling and risk assessment. Emphasizing the potential risks associated with unnecessary OCP use – particularly unsupervised short-term usage for non-medical reasons – may help promote safer practices and ultimately reduce the incidence of CVST.

By elucidating the multifactorial nature of risk factors in CVST, our findings underscore the importance of comprehensive patient history assessment and risk stratification in clinical practice. This holistic approach can enhance preventive strategies and targeted interventions.

Fasting was noted in 9.4% of our patients, which is consistent with the findings of Ghiasian et al., who conducted their study in Hamadan City, Iran, where fasting and subsequent dehydration were suggested as contributing factors to CVST.[23] The multifactorial nature of common characteristics in our study, with many patients presenting with more than one predisposing factor, echoes the results of Yadegari et al., who found that 36% of their patients had multiple contributing factors.[22] Recognizing fasting as a potential risk factor highlights the need for increased awareness, especially during religious observances, to mitigate dehydration-related complications.

Mortality rates in patients with CVST have shown considerable variability across studies. The present study reported a relatively low mortality rate, consistent with a report from Tehran City, Iran, which found a mortality rate of 3.7%.[22] In contrast, the study of Ghiasian et al. indicated a significantly higher mortality rate of 16.9%.[23] The variations in mortality rates across studies indicate disparities in healthcare access, quality of care, and timeliness of diagnosis and treatment. Understanding these differences can inform targeted interventions and resource allocation to improve outcomes in regions with higher mortality rates.

The cumulative data analysis in Iran reported an overall mortality rate of 11.4%, suggesting that outcomes may differ based on regional healthcare facilities and access to timely intervention.[14] Mortality rates of 22.58% were observed in the study from Central India, underscoring the critical importance of early diagnosis and management in CVST cases.[24] These findings highlight the urgent need for strategies aimed at enhancing early detection and treatment protocols for CVST. Developing region-specific guidelines could significantly improve survival rates and overall patient prognosis.

This study has several limitations. First, the absence of a control group precludes any causal inference regarding the observed associations. Second, our findings are based on hospital-based registry data from two referral centers, which may not fully represent the general population and could introduce selection bias toward more severe or complex cases. Third, the relatively small sample size limits the precision of our estimates and may reduce the ability to detect less common clinical features. Finally, the retrospective design carries inherent risks of incomplete documentation, misclassification, and reliance on

available medical records, which could affect the accuracy and completeness of data.

The results of the current study should be interpreted with caution, as the use of a hospital-based registry may introduce selection bias and fail to capture cases from the broader community. Moreover, misclassification bias is possible due to retrospective ascertainment of exposures from medical records and self-reports. Attrition bias may have also occurred from losses to follow-up, although follow-up rates remained high. In addition, information regarding the type of treatment including anticoagulation use, neurosurgical interventions, or use of thrombolysis/thrombectomy was not available in this study. These treatments influence outcome, and their absence limits interpretation. Finally, time intervals between onset, admission, anticoagulation, and imaging are important prognostic variables, which were not reported in this study. Therefore, the outcomes should be interpreted cautiously.

Conclusion

This study describes the clinical features, common exposures, and outcomes of patients with CVST in northwestern Iran. Headache was the most common presentation, and OCP use and fasting were frequent exposures. Most patients achieved good functional outcomes at follow-up. Future population-based and controlled studies are required to assess true risk factors and incidence of CVST in Iran.

Conflict of Interests

The authors declare no conflict of interest in this study.

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