

A SIX-MONTH STUDY OF CLINICAL SYMPTOMS, IMAGING AND OUTCOMES OF PATIENTS DIAGNOSED WITH CEREBRAL VENOUS SINUS THROMBOSIS (CVST)

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ABSTRACT

Background: One of the unusual cause of headache and stroke is CVST with very diverse clinical manifestation. Onset of focal headache, headache with seizures, papilledema, or focal defect are some of important clinical features. Consideration of risk factors, especially the use of hormonal drugs, recent pregnancy, coagulation disorders, as well as recent infections and systemic inflammation, can lead to clinical suspicion of CVST. For early and accurate detection we can use modern MR imaging.

Objective: To evaluate the clinical symptoms and imaging findings of patients with a diagnosis of CVST during 6-months follow-up.

Methods: This cross-sectional study was used on 56 patients with CVST. Clinical, preclinical, and imaging records of inpatients and also information like age, sex, and underlying diseases were collected at a checklist. After 6 months from the start of treatment, the identified patients were followed up through a telephone interview, and if there were any positive symptoms, they were visited on an outpatient basis in the neurology clinic of Alavi Hospital in Ardabil, and the necessary information was extracted. Collected data were analyzed by statistical methods in SPSS version 21.

Results: Of all patients, 47 (84%) were women. The most common symptom was headache with 87.5% and then nausea and vomiting, sensory and visual symptoms with 57.1%, 51.8% and 44.6%, respectively.

Conclusion: The results of this study showed that, the clinical symptoms of patients are very various and misleading, but the most common clinical symptoms were headache, nausea and vomiting. Women were involved more than men. The results of the study disclosed that CVST had wide range of clinical manifestations and non-specific symptoms at the beginning. For that reason, in especially high risk groups for thrombosis, the diagnosis of CVST should be kept in mind.

Keywords: Cerebral Venous Sinus Thrombosis, MR-Venography, Anticoagulant Therapy, SII, Modified Rankin Scale

Introduction

One of the rare cerebrovascular diseases was CVST which accounts for 1% of all cerebrovascular events, but the mortality rate is as high as 10.¹⁻² Cerebral venous sinus thrombosis (CVST) is an uncommon cause of stroke, with an annual incidence of about 5 million people.³⁻⁵ This complication can affect all age groups, so the disease has been reported from the age of 6 days to 77 years. The average age of the disease is 33 years, and its incidence is higher in women.⁶⁻⁸ The clinical manifestations of this disease are different and therefore can delay the diagnosis.⁹ Patients can experience headache, papilloedema, focal disturbances, seizures, and coma. Its most common symptom is severe headache.¹⁰ It can be broadly divided into the following four main syndromes: (1) increased intracranial pressure, (2) focal cerebral dysfunction, (3) encephalopathy, and (4) seizures with or without focal neurological deficits. Various

causes can cause sinus thrombosis that the first of which are infectious causes (microbial, viral, fungal, and parasitic) and then hormonal causes including pregnancy, postpartum, use of birth control pills, use of androgens, abortion, cancers (adenocarcinoma). Pancreas, lung, breast, lymphoma, leukemia, metastasis), blood disorders, systemic diseases (nephrotic syndrome, polyarthritis nodosa, Wegener, Behcet, ulcerative colitis), trauma, drugs and dehydration can be mentioned.^{6-8,12-14} In recent years, computed tomography (CT) and magnetic resonance imaging (MRI) have been increasingly used, and they help doctors in the field of CVST diagnosis, even in cases with atypical manifestations.⁴ The most sensitive diagnostic method is the use of MRI in combination with magnetic resonance venography.¹⁵⁻¹⁶ MR venography is often used to examine the intracranial venous system, especially in the evaluation of dura mater sinus thrombosis.¹⁷ Electroencephalography (EEG) records brain findings and is used to diagnose brain

diseases.¹⁸ Electroencephalography (EEG) is the most specific method to determine the epileptogenic cortex. Its sensitivity and specificity depend on various factors, including age and stages of recording, such as sleep recording and activation methods (hyperventilation, light stimulation).¹⁹ Seizures are one of the main symptoms of cerebral venous thrombosis (CVT), but predictive factors for seizures are still unknown.²⁰ Since the EEG has been developed as a valuable tool for studies of brain activity, evidence has accumulated that there is a close but complex relationship between brain electrical activity, metabolism, and cerebral blood flow. Although there is still no comprehensive explanation of the neurophysiological basis of EEG, it has been proven that abnormal frequency and wave patterns indicate various pathological conditions in the brain. These experimental findings have led to the general use of EEG as a diagnostic tool with many clinical and laboratory applications.²¹ The goals of anticoagulant treatment in venous sinus thrombosis are: 1) to re-canalize the closed vein or sinus 2) to prevent the spread of thrombus 3) to prevent pulmonary embolism 4) to treat the prothrombotic underlying condition in a person. Various studies showed that this disease is of great importance and has significant mortality and morbidity. Also, most of the affected patients are in young age groups, so choosing a suitable and affordable modality in line with early diagnosis for the patients of this hospital is the priority of our work, and it made us to investigate the diagnostic and treatment process in sinus thrombosis patients. A vein referred to Alavi Hospital in Ardabil, we evaluated the management of these patients and chose the best and most standard treatment method with the least cost and the best outcome to improve the disease prognosis in these patients. The purpose of this study was to evaluate the clinical symptoms and imaging findings of patients with a diagnosis of CVST during 6-months follow-up.

Methods

This descriptive cross-sectional study was conducted on 56 patients diagnosed with CVST who referred to Ardabil city hospital during 2018-19. The diagnosis of venous sinus thrombosis was based on examination, CT scan and MRI and was confirmed by observing the lesion in the sinus veins by MR venography. In each of the patients, the main complaints, clinical findings, imaging findings, location of thrombosis in the venous sinus, changes in electroencephalography, and any history of taking predisposing drugs for thrombosis were reviewed and recorded. Also, the demographic characteristics of the patients, including: age, sex, and underlying diseases were also collected. After 6 months from the start of treatment, the identified patients were followed up through a telephone interview, and if there were any positive symptoms, they were visited on an outpatient basis in the neurology clinic of Alavi Hospital in Ardabil, and the necessary information was extracted. The collected data through checklists were analyzed in SPSS software version 21. At first, 88 patients with primary diagnosis of venous sinus thrombosis were collected which of them, 15 patients due to non-diagnosis of CVST and 17 patients due to lack of sufficient information

in their file were excluded from the study. The study was registered by ethics code IR.ARUMS.REC.1399.340.

Results

Table 1. Findings of imaging types in the studied patients

Imaging type	Abundance	Percentage
CT Scan		
Hyperdensity of cortical veins or sinus dura	17	30.4
Infarct normal	1	1.8
	38	67.8
M.R.I		
signal change	37	66.1
normal	19	33.9
MRV		
No signal	44	78.5
narrowing	7	12.5
Hypoplasia	5	8.9

Table 2. Coagulation tests in patients

Variable	Low		Normal		High	
	n	%	n	%	n	%
ANA	-	-	32	97	1	3
dsDNA	-	-	-	-	-	-
Homocysteine	1	3	29	88	3	9
AntiThrombinIII	2	6	31	94	-	-
Protein S	-	-	33	100	-	-
Protein C	2	6	31	94	-	-
Cardiolipin	2	6	31	94	-	-
ANCA	2	6	31	94	-	-
FANA	2	6	31	94	-	-
β ₂ microglobulin	2	6	31	94	-	-
Antiphospholipid	2	6	31	94	-	-
CH50	2	6	31	94	-	-
Complement C3	2	6	31	94	-	-
Complement C4	2	6	31	94	-	-

Table 3. Laboratory tests of examined patients.

Variables	Average	SD
WBC	18016.1	2583.3
Hb	13.01	2.2
Plt	251553.57	83148.6
PT	12.58	1.1
PTT	27.08	3.4
INR	1.17	0.41
Cr	0.85	0.21
BUN	29.59	14.44
ESR	20.14	11.99

A total of 56 patients diagnosed with venous sinus thrombosis were examined. 9 patients were male (16%) and 47 patients (84%) were female. The most age group was related to 25-29 years with 19.6%. The average age of all patients was 40 ± 15.3 . 39 patients (70%) had an underlying disease, the most common of which was blood pressure with 17.4% (Figure 1).

18 patients (32.1%) were not taking any specific medication and the rest of the patients were being treated with medication. In the studied patients, the most common clinical symptom was headache with a frequency of 49 patients (87.5%) (Figure 2).

In this study, three imaging methods were used step by step for patients. First, a brain CT scan was performed for the patients, then an MRI was performed to examine the soft tissue and the causes of the symptoms,

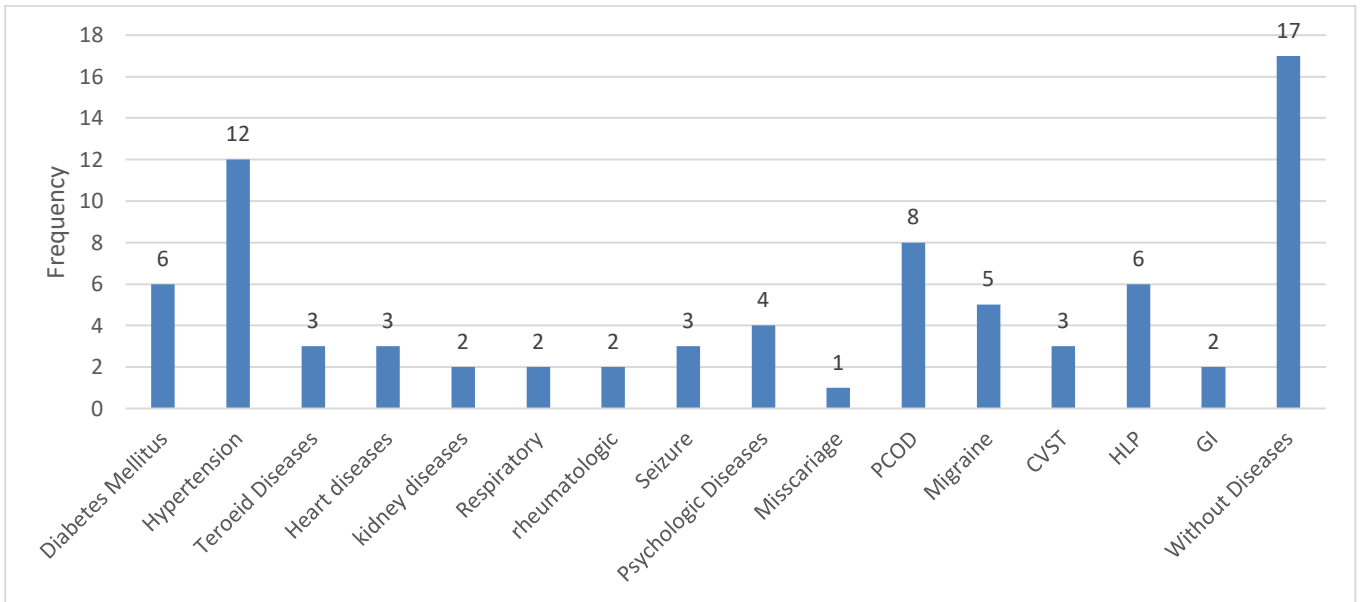


Figure 1. Frequency of underlying diseases in the studied patients

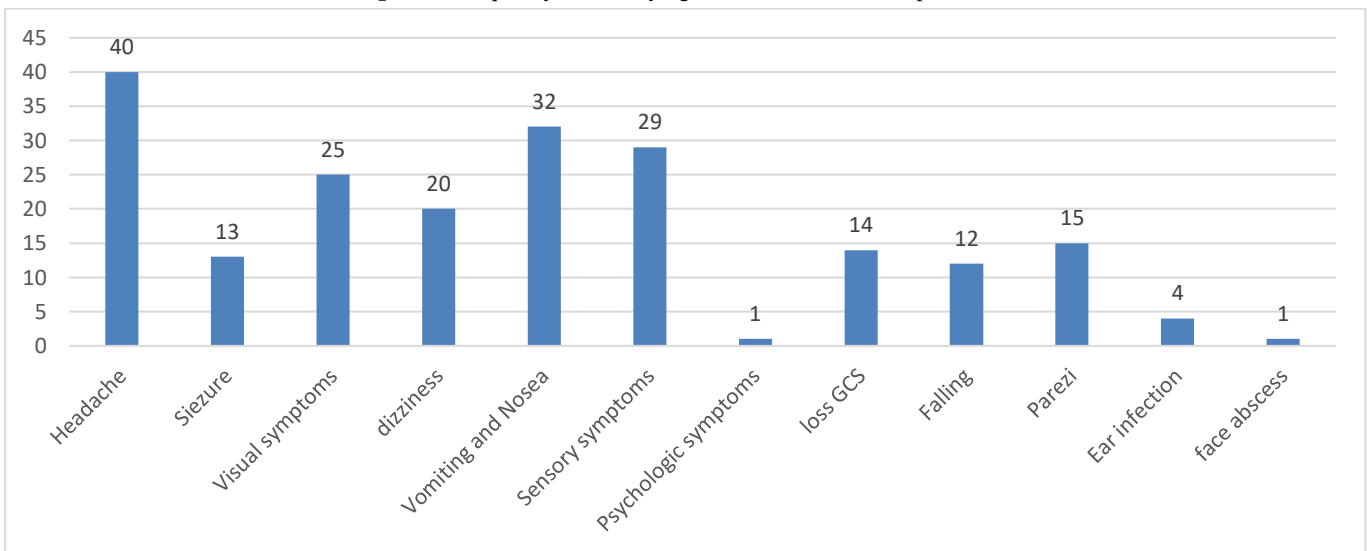


Figure 2. Symptoms and clinical findings in the studied patients

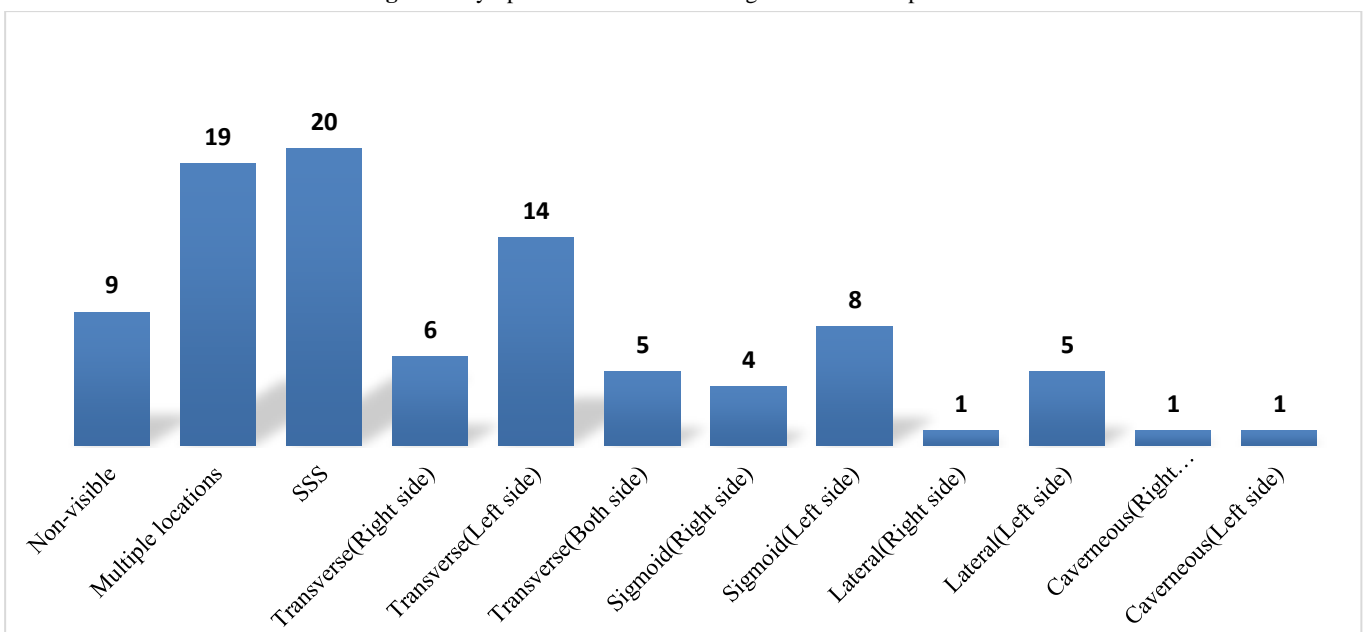


Figure 3. Frequency of involvement of venous sinuses in the studied patients

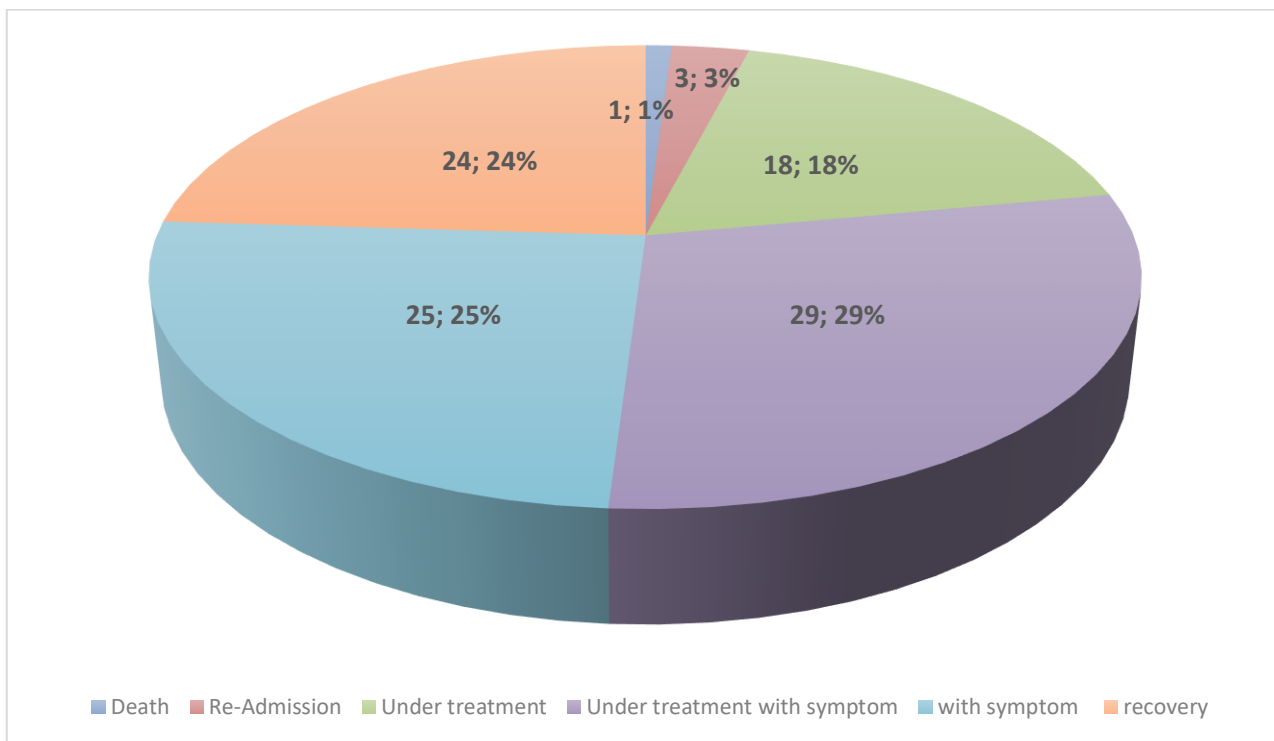


Figure 4. Status of the studied patients during the six-month follow-up

and at the end, an MR-Venography was performed to examine the venous sinuses and confirm the diagnosis of venous sinus thrombosis. 18 patients (32.2%) had an abnormal CT scan (Table 1).

Among the 56 patients studied, only 33 (58%) of the patients had the necessary tests to check the coagulation status of the body. Three patients (9.1%) had homocysteine and 1 patient (3%) had high ANA levels (Table 2). The average Hb in patients was 2.2±13 (Table 3).

In the imaging studies of patients with MRV method, the upper sagittal sinus has the most frequency of involved sinuses among patients with 37.5% (Figure 3).

During the six-month follow-up of the studied patients, clinical symptoms had improved in 26 patients (46.4%). 1 (Figure 4). The most cases of conflicts were in summer with 19 people (33.9%) and in September with 10 people (17.9%).

Discussion

In the current study, 56 patients diagnosed with venous sinus thrombosis were studied. The greatest number of which with 47 (84%) was women. In 2017, Gazioglu et al examined 50 patients with venous sinus thrombosis. In their study, 39 patients (78%) were women, and the rest (22%) were men. Also, in the study of Jangharbani et al. in 2007, which was conducted in Isfahan city on 122 CVST patients, 96 (78.7%) of the patients were women, which shows that the results of our study are similar to the results of both previous studies.²²⁻²³

In our study, the clinical symptoms of the patients ranged from neurological symptoms such as headache and blurred vision to psychological symptoms such as apathy. The most observed symptom in the patients was headache with 87.5%, nausea and vomiting with 57.1%, sensory symptoms with 51.8% and then visual symptoms with 44.6%. In 2017, C. Anadure et al. examined clinical symptoms and MRI

findings in 54 patients diagnosed with venous sinus thrombosis in a prospective observational study. In their study, clinical symptoms included headache (94%), nausea and vomiting (62%), seizures (42%) and neurological deficits (33%) in order of frequency and prevalence. In this mentioned study, similar to the present study, headache and nausea and vomiting were the most common symptoms in patients, but the prevalence of seizures was higher in their study.²⁴

The most common risk factors were OCP consumption in 13 of 47 female patients (27.6%), PCOD in 13.47 (17%), complement C3 deficiency in 4.33 (12.5%) and ear infection in 4.56 (11.1%). 7%) was obtained. In the study of S. Devasagayam et al. in 2016, which was conducted retrospectively on 105 patients diagnosed with CVTS who were hospitalized between 2005 and 2011, and in the examination of the results related to risk factors, like our study, the most common risk factor was consumption. OCP tablets were present in 17 of 54 women (31%).⁹ In the study of E. Terazzi et al. in 2005, which was conducted as a multicenter study in 11 centers and during 4 years, 48 patients were examined. The rate of OCP consumption was 47.4% in female patients, 8 (16.7%) had a previous history of venous thrombosis and 4 (10.5%) had a history of miscarriage. In examining the coagulation status of people, hyperhomocysteinemia in 3 people (11.5%), disorder in protein C and disorder in protein S in each of 2 people (7.7%), and disorder in antithrombin factor III in 1 person (8 /%3) was present.²⁵ In a retrospective cohort study in Helsinki, Finland, J. Putaala et al examined 91 CVST patients. The risk factors reported in their study in order of frequency included: OCP use in 34 people (53%), head and neck infection in 20 people (22%), history of previous thrombosis in 10 people (11%), rheumatological drugs in 10 (11%), pregnancy and puerperium in 7 (8%), systemic inflammatory causes as well as hyperhomocysteinemia in 4 (4%), antiphospholipid antibody disorder in 1 (1%) (26), in

which Similar to the present study, the most common risk factor for OCP use was the same, but contrary to the results of our study, infections were more common than coagulation and hormonal disorders. In our study, in the CT scan of the patients, 17 patients (30.4%) had hyperdensity of veins and venous sinuses, in the MRI findings, 37 patients (66.1%) showed evidence of signal change to The benefit of infarction was found. In vascular examination by MRV, absence of signal was evident in 44 patients (78.5%). In the observational prospective study that C. Anadure et al. conducted in 2017 on 54 patients diagnosed with venous sinus thrombosis, in terms of clinical symptoms and MRI findings, 37 patients (68%) had venous infarction in MRI. 17 people (32%) had only cortical and dural thrombosis without brain parenchymal involvement, which results were the same and consistent with our study.²⁴

In the results of MRV imaging in the studied patients, the location of the involved sinuses was checked, and the most common sinus involved was the upper sagittal sinus with a frequency of 20 cases (35.7%), followed by the right transverse sinus and the right sigmoid sinus, respectively. The frequency was 14 cases (25%) and 8 cases (14.3%). In 19 cases (33.9%) several sinuses were involved and in 9 cases (16.1%) the site of involvement in the sinuses was not known.

In 2019, Hashmi et al., in a two-center retrospective study in Oman, examined 54 CVST patients, and in the analysis of the imaging results, 21 cases (38.9%) had involvement in multiple sinuses, 19 cases (35.2%) were involved in the location of the sigmoid and/or transverse sinuses, and involvement of the superior sagittal sinus was observed in 9 cases (16.7%)²⁷, which was contrary to the results of our study and the involvement of the sigmoid and transverse sinuses more than the superior sagittal sinus had occurred.

In the present study, the investigated patients were followed up in terms of symptoms, mortality and morbidity and re-hospitalization during 6 months and their follow-up results showed that recovery was achieved in 26 cases (46.4%). Also, in the follow-up done for the Modified Ranken Scale patients, it was calculated that 51 cases (91.1%) scored zero, 3 cases (5.4%) scored 1, one case (1.8%) scored 2 and one case (1.8%) received a score of 6. In the study of E. Rezoagli and colleagues in 2018, they studied 508 CVT patients. And in the follow-up of patients six months after the onset of symptoms, 78.5% of patients had complete recovery (mRS=0). 19% of patients had minor symptoms (mRS=1) and it was in 2.1% of patients (mRS=2). It was in 1.1% of patients (mRS=3) and finally 2.1% had mRS 3.²⁸ Ferro et al. in 2004 in a multi-national (21 countries) multi-center (89 centers) prospective observational study of 624 patients during the years 1998 to 2001 and followed up. In the six-month follow-up of patients, the MRS criteria in 284 cases (46.1%) had score zero, 197 cases (32%) score 1, 49 cases (8%) score two, 24 cases (3.9%) score three. 16 cases (2.6%) had a score of 4, four cases (0.6%) had a score of 5, and 42 cases (6.8%) had a score of 6, which indicates death. In this study similar to the present study, most patients received a score of zero, and in the follow-up, recovery was the most common finding in both studies.¹⁰ In our study, the prevalence of the disease in the summer season with 33.9% and in the month of September with 17.9% was the most conflict. Jangharbani et al studied 122 patients in a

prospective study between 2001 and 2004. In examining the seasonal distribution pattern and by month in this study, the highest distribution is in autumn and in September with a frequency of 45 cases (35.2%) and 21 cases (17.2%), respectively.²³

Limitations of the study

Due to the weak cooperation of the patients to perform control MRV in the follow-ups performed in this study, it was not possible to check the status of re-canalization in the performed follow-ups.

Conclusion

Conducting similar studies over a longer period of time and with a larger statistical population and in other medical centers, examining other inflammatory markers such as LDH and D-dimer, more fully examining coagulation factors, examining the EEG of patients with CVST and evaluating EEG diagnostic findings. , a more detailed and thorough examination of prognostic criteria such as SII and MRS to evaluate the sensitivity and accuracy of these criteria in predicting the complications and outcome of patients, as well as examining the recanalization status of the involved sinuses during follow-up by MRV control is suggested for future studies.

Acknowledgement

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Conflict of Interest

None.

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