

Outcomes of Cerebral Venous Thrombosis in Al-Yarmook Teaching Hospital

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Abstract

Background: Cerebral venous thrombosis (CVT) is a disease with multiple causes and has a low incidence rate. Seizure is one of the most common complications of CVT. The rate at which seizure occurs following CVT and the risk factors associated with that occurrence is a debated issue. **Objectives:** The aim of this study was to evaluate the incidence of seizure and its associated and risk factors for patients with CVT. **Subjects and Methods:** This was an observational study that included a total of 30 adult patients with CVT. Data, including age, sex, clinical manifestations such as fever, headache, vomiting, altered consciousness, and focal neurologic signs, such as sensory disturbances, were collected. Imaging findings that included hemorrhagic lesion, infarction, and thrombus site were also reported. Patients were followed up for 6 months from the initial diagnosis to recognize the development of seizures. **Results:** Within 6 months of follow-up, 13 (43.3%) patients developed generalized seizures, which was the most common type of CVT. The superior sagittal sinus (SSS) occlusion was recognized in 84.62% of patients with seizures and 48.06.5% in patients without seizures. Similarly, the right lateral sinus was occluded in 84.62% of patients with seizures as compared with 41.18% among those without seizures. Contraceptive use was reported in 61.54% of patients with seizures versus 17.65% in those without seizures with a significant difference. **Conclusion:** The involvement of SSS and lateral right sinus occlusion and use of contraceptives could be warning signs and a risk factor for the development of seizures in patients with CVT.

Keywords: Cerebral venous thrombosis, risk factors, seizures, thrombus

INTRODUCTION

Cerebral venous thrombosis (CVT) is a rare form of cerebrovascular disorders that mainly affect young adults.^[1] Although CVT is responsible for only 0.5%–1% of all strokes,^[2] its sequelae are usually devastating if no proper measures are taken. Recognized risk factors for CVT comprise pregnancy or puerperium, using oral contraceptive pills (OCP), and coagulopathies. Therefore, most of affected patients are of the female gender.^[1]

Presenting symptoms are varying widely and include progressive headache and vomiting, focal neurological deficits, and various degrees of disturbance in consciousness as well as mental symptoms. In addition, epileptic seizures are a common and important clinical manifestation of CVT, occurring in approximately one-third of the affected patients.^[3] It was previously reported as a first sign in 29% of the patients with CVT, with

approximately 60% of these cases having generalized seizures.^[4] On the contrary, secondary epileptic seizures were frequently recognized as important risk factors for short-term death in such patients.^[5,6] In particular, the secondary seizures are important to evaluate the survival in patients with CVT. Only few studies have addressed the factors associated with the development of epileptic seizures in patients with CVT.^[7,8] Determining such factors may help the clinicians to decide the proper treatment and prophylactic antiepileptic drugs, therefore reducing the possible harm of seizures.^[8] Thus, this study aimed to

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evaluate the risk factors for developing epileptic seizures in a sample of Iraqi patients with CVT.

SUBJECTS AND METHODS

This was a case series observational study, which was conducted at Al-Yarmook Teaching Hospital. The study included a total of 30 adult patients 18 years of age or older who were admitted to our center with cerebral venous sinus thrombosis from March 2017 to March 2018. The diagnosis was suspected based on the symptoms, for instance, the presence of each of headache, increased intracranial pressure, and focal neurological abnormalities. Magnetic resonance imaging (MRI) with venography was used to confirm the diagnosis. The inclusion criteria of the study included all patients aged over 18 years who were eligible for treatment with an oral anticoagulant. The exclusion criteria of the study included patients having CVT associated with central nervous system (CNS) infection or due to head trauma, those planned for surgical treatment for CVT, those receiving anticoagulant treatment for an indication other than CVT and requiring continuation of that treatment, and those with severe renal impairment, active liver disease, pregnancy, nursing, or planning to become pregnant.

Data collection

Patient's interview or medical records were used to retrieve the following data on standardized datasheet: age, sex, clinical manifestations according to history, and physical examination, including fever, headache, vomiting, altered consciousness, and focal neurologic signs, including weakness and sensory disturbances. Imaging findings included bleeding, infarction and number, and location of thrombus. Furthermore, data regarding duration of symptoms, duration of hospitalization, puerperium, presence of tumor, using of OCP, and dehydration were also collected.

All study subjects had received subcutaneous low-molecular-weight heparin (nadroparin calcium 0.1 mL/10 kg, once per 12 h) for a maximum of 14 days, and oral warfarin thereafter as an anticoagulant therapy. Warfarin dose was set based on the international normalized ratio (INR 2–3).

Six-month period was assigned to follow the patients during which the development of epileptic seizure was detected. The Guidelines for Epidemiologic Studies on Epilepsy formulated by the International League Against Epilepsy was adopted for diagnosis and classification of epileptic seizures.

Data analysis

Descriptive statistics were performed to analyze the patients with CVT with and without epileptic seizures. For continuous variables, means and standard deviation (SD) were calculated. For categorical variables, numbers

and percentages for each category were tabulated. All variables were compared between patients with seizures versus without seizures using Student's *t* test for continuous variable and chi-square test/Fisher's exact test for categorical variables. A significant difference was set at $P < 0.05$. Data were analyzed by using Statistical Package for the Social Sciences (SPSS) software program, version 13.0 for Windows.

RESULTS

Baseline demographic and clinical characteristics of patients

Mean age of the patients in this series was 36.1 ± 13.8 years (range 18–67 years). Males represented only 40% of the patients. Duration of symptoms was 8.4 ± 6.1 days (range 2–13 days) with an average hospital stay of 7.2 ± 5.9 (range 1–13 days).

Headache was so far the most prevalent symptom observed in 93.33% of patients, whereas sensory deficit was the least prevalent symptom (20%). In between, there was a list of symptoms, the most frequent symptoms of them were confusion (60%), visual impairment (26.67%), and motor deficit (26.67%). Interestingly, none of the patients had seizure at presentation.

Two imaging findings, hemorrhagic lesion and infarction, were encountered, which represented 16.67% and 23.33%, respectively [Table 1].

The superior sagittal sinus (SSS) was the most involved sinus (63.33%) followed by the right lateral sinus (60%), whereas deep vein system was the least involved (10%). It is obvious that more than one sinuses were involved in many cases. The most common risk factors were the contraceptive and puerperal periods, which were associated with 16.67% and 13.33%, respectively, of the patients.

Incidence of epileptic seizures in patients with cerebral venous thrombosis

Within 6-month follow-up, 13 (43.3%) patients developed epileptic seizure, whereas 17 (56.67%) did not [Figure 1].

Types of epileptic seizures

As for seizure type, four (13.33%) patients had only focal seizures, three (10%) experienced focal seizures and secondary generalized seizures, and six (46.15%) suffered generalized seizures [Figure 2].

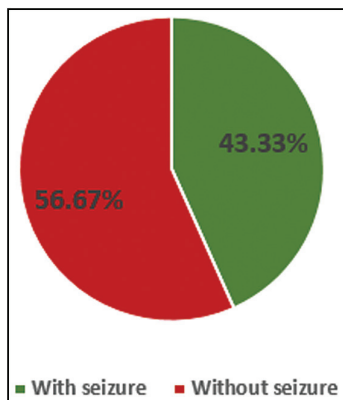
Association of demographic and clinical characteristics with the development of epileptic seizures in patients with cerebral venous thrombosis

No significant differences were observed between CVT patients with and without epileptic seizures in terms of age, duration of symptoms, and duration of hospitalization [Table 2]. Regarding presenting symptoms, confusion was

Table 1: Baseline demographic and clinical characteristics of patients

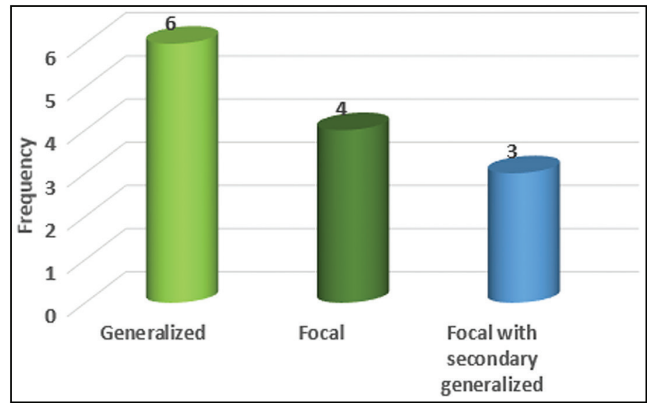
Variables	Frequency(%) or mean $\pm$ SD
Age, years	36.1 $\pm$ 13.8
Gender	
Male	12(40%)
Female	18 (60%)
Duration of symptoms, days	8.4 $\pm$ 6.1
Duration of hospitalization	7.2 $\pm$ 5.9
Presenting symptoms	
Headache	28(93.33%)
Confusion	18(60%)
Visual impairment	8(26.67%)
Motor deficit	8(26.67%)
Sensory deficit	6(20%)
Imaging findings	
Hemorrhagic lesion	5(16.67%)
Infarction	7(23.33%)
Occluded sinus/vein	
Superior sagittal sinus	19(63.33%)
Right lateral sinus	18(60%)
Left lateral sinus	15(50%)
Intracranial vein	15(50%)
Risk factors	
Oral contraceptive	5(16.67%)
Puerperium	4(13.33%)
Dehydration	2(6.67%)
Malignancies	1(3.3%)
Death	1(3.33%)

SD = standard deviation

**Figure 1:** Percentage of patients with cerebral venous thrombosis who developed an epileptic seizure

observed in 92.31% of patients with seizures as compared with 35.29% in patients without seizures. According to imaging findings, neither hemorrhagic lesion nor infarction showed a significant association with the occurrence of seizure.

Of four sites for thrombosis, two differed significantly between patients with and without seizures. SSS occlusion was observed in 11 patients with seizures (84.62%), whereas only 8 (48.06.5%) of patients without seizures

**Figure 2:** Frequency of different types of seizure in patients with cerebral venous thrombosis

were recognized to have the involvement of this sinus. Similarly, the right lateral sinus was occluded in 11 (84.62%) of patients with seizures as compared with 7 (41.18%) among those without seizures.

The only included risk factor which appeared to have a significant association with the development of epileptic seizure was the using a contraceptive which reported in 8 (61.54%) of patients with seizure versus 3(17.65%) in those without seizures.

DISCUSSION

This study aimed to investigate the occurrence and risk factors associated with epileptic seizures in patients with CVT. One of the most interesting results in the current series is the relatively high incidence of CVT among Iraqi population. During a period of 1 year within single center, there were at least 30 patients with confirmed CVT. Compared with other international studies, in Qatar, Algherbawe *et al.*^[9] collected 43 cases during 4 years and in Tukey Gunes *et al.*^[11] had 10 years' time period to gather 75 cases. This high incidence in Iraq necessitates a prompt investigation to find out the behind etiologies.

Mean age of the patients with CVT in this study was 36.1 $\pm$ 13.8 years which is comparable with most previous studies. In an international multicenter study of 11,400 hospitalized patients with CVT, Nasr *et al.*^[10] reported an average age of 38.1 years. Interestingly, some studies reported even younger ages than these studies. For example, Haghighi *et al.*^[11] retrospectively investigated 465 Iranian patients with confirmed CVT and showed that their mean age was 29.52 $\pm$ 34.8 years.

The current series revealed that females were more affected by CVT than males (male-to-female ratio was 1:1.3). This result is in accordance with several previous series. In a retrospective study including 69 patients with CVT, Sha *et al.*^[8] found that female patients represented 55.07%. Patil *et al.*^[12] performed a retrospective study on 50 patients and found that 42% of whom were males and 58% were females.

Table 2: Association of demographic and clinical characteristics with the development of seizures in patients with cerebral venous thrombosis

Variables	With seizure (n = 13)	Without seizure (n = 17)	P Value
Age	39.43 ± 14.1	33.3 ± 12.7	
Gender			
Male	6 (46.15%)	6 (35.29%)	0.547
Female	7 (53.85%)	11 (4.71%)	
Duration of symptoms, days	9.2 ± 4.9	7.7 ± 5.2	0.184
Duration of hospitalization	8.1 ± 4.4	6.4 ± 4.5	0.119
Presenting symptoms			
Headache	12 (92.31%)	16 (94.12%)	0.844
Confusion	12 (92.31%)	6 (35.29%)	0.002
Visual impairment	4 (30%)	4 (23.53%)	0.657
Sensory deficit	3 (23.08%)	3 (17.65%)	0.713
Motor deficit	5 (38.46%)	3 (17.65%)	0.201
Imaging findings			
Hemorrhagic lesion	4 (30.78%)	1 (5.88%)	0.07
Infarction	3 (23.08%)	4 (23.53%)	0.977
Occluded sinus/vein			
Superior sagittal sinus	11 (84.62%)	8 (46.06%)	0.034
Left lateral sinus	7 (53.85%)	8 (46.06%)	0.713
Right lateral sinus	11 (84.62%)	7 (41.18%)	0.016
Intracranial vein	8 (61.54%)	7 (41.18%)	0.269
Risk factors			
Puerperium	2 (15.38%)	2 (11.76%)	0.773
Malignancy	1 (7.69%)	0 (0%)	0.245
Oral contraceptive	5 (38.46%)	0 (0%)	0.027
Dehydration	0 (0%)	2 (11.76%)	0.201
Local infection	1 (7.69%)	2 (11.76%)	0.713

Bold values are significant at 0.05

The most common symptom in this study was headache that affected the vast majority of patients (93.33%). Confusion came next affecting 60% of the patients. Globally, there is almost a general consensus among different studies that the headache is the most common symptom in patients with CVT, although the percent varies from 62% to 97%.^[13]

Two imaging findings, hemorrhagic lesion and infarction, were encountered in this study, which represented 16.67% and 23.33%, respectively. Almost in accordance with this result is the study of Ding *et al.*^[7] who found that hemorrhagic venous infarction was the most common MRI finding accounting for 30% of cases. Also similar observations were reported by Banaker and Hiregoudar.^[14]

SSS was found to be the most affected sinus in this study (63.33%), a result that is in accordance with most previous studies in this issue.^[12] Even though, some studies found the transverse sinus was the most affected one.^[1,15] The involvement of these two sinuses is due to their normal function as the major dural sinuses that receive a considerable amount of venous drainage in the CNS.^[16]

The most common risk factors for CVT encountered in this study were oral contraceptive (in 16.67% of cases and

puerperium in 13.33% of cases). This in accordance with a recent meta-analysis, which confirmed that OCP can significantly increase the incidence of CVT in women at reproductive age.^[17]

Only one patient had died in this study which is lower than that reported in International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) study^[3] which was 4.3% and Haghighi *et al.*^[11] study (4.4%), and higher than Ding *et al.*^[7] study (2%).

In the current series, 13 (43.3%) patients with CVT have developed epileptic seizures with 6-month follow-up period. This result is comparable with many other previous studies. Patil *et al.*^[12] reviewed the hospital records of 50 Indian patients with CVT and reported that 21 (42%) of them had developed epileptic seizures. In China, Sha *et al.*^[8] showed that out of 69 patients with CVT, 32 (46.38%) patients had experienced secondary seizures.

In fact, there is a complete agreement between researchers about the role of CVT as a cause of epileptic seizures, but the frequency of seizures after CVT is a debate issue. The variation in this frequency is justifiable because a large number of factors such as age, pregnancy, comorbidities, and infections have a role in this regard.

Generalized seizure accounted for the vast majority of epileptic seizure cases in this study. This is in agreement with the most previous studies. In Ding *et al.*'s^[7] study, generalized seizure was reported in 69.21%, focal in 13.5%, and focal with secondary generalized in 11.5%. Anadure *et al.*^[15] reported the incidence of generalized, focal, and focal with secondary generalized seizure in patients with CVT 65%, 25%, and 10%, respectively. Nevertheless, some studies reported somewhat different results. In the study of Kalita *et al.*,^[18] seizures were categorized as focal in 26.19%, focal with secondary generalized in 45.24%, and generalized in 38.1%. There were 10 patients with generalized convulsive status epilepticus.

In this study, confusion was significantly more frequent in patients with seizures than those without seizures. This result is in agreement with the study of Ding *et al.*^[7] who found that confusion was significantly associated with CVT patients who developed epileptic seizure as compared with those who did not develop epileptic seizure regardless of the type of seizure.

Regarding the site of thrombosis, SSS and right lateral sinus occlusion was observed more frequently in patients with seizure than those without seizures with significant differences. These results are completely in agreement with Patil *et al.*^[12] who reported that involvement of SSS and right lateral sinus were mostly frequently associated with the development of seizure. The SSS is the main vessel that drains blood from the supratentorial parenchyma. A recent study by Davoudi *et al.*^[19] showed that this region (supratentorial parenchyma) is the only location in the CNS that independently correlated with development of epileptic seizures. This explains the significant association of SSS occlusion with the development of seizure in patients with CVT.

Of four risk factors included in this study, only OCP showed a significant association with development of seizures in patients with CVT. This result is in agreement with Davoudi *et al.*^[19] who reported that OCP can predispose for seizure development in patients with CVT.

A key limitation of this study was that it is a single-center study with a relatively low sample size. Another limitation was that we were not able to assess treatment effects of antiepileptic drugs for patients who developed seizure.

Collectively, these data alert the high incidence of CVT among Iraq patients, and suggest that the involvement of SSS and lateral right sinus occlusion may be warning signs for the development of epileptic seizures in patients with CVT, whereas using of contraceptives could be a risk factor for development for such a development.

Ethical policy and institutional review board statement

This study was approved by Institutional Review Board (IRB) by the Iraqi Board for Medical Specializations.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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