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Original article

Predictors and Outcomes of Status Epilepticus in Patients with Cerebral Venous Thrombosis

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Abstract:

- ***Background*:** Status epilepticus (SE) is a serious complication of cerebral venous thrombosis (CVT). However, the risk factors associated with the development of SE and its impact on outcomes remain a subject of ongoing debate. This study aimed to identify predictors of SE in patients with CVT and to assess the relative risk of SE in contributing to mortality and disability compared with CVT patients without SE.
- ***Methods:*** This was a comparative case series study involving 29 patients with CVT admitted to Al-Yarmouk Teaching Hospital between January 2019 and March 2021. Patients were followed up and re-evaluated at 3 and 6 months post-discharge. Outcomes were assessed using the modified Rankin Scale (mRS).
- ***Result:*** Of the 29 CVT patients, 11 (37.9%) developed SE. Significant predictors of SE included decreased level of consciousness (GCS ≤8; p = 0.0001), motor weakness (p = 0.003), and the presence of supratentorial lesions on brain MRI, particularly hemorrhagic lesions (p = 0.003). At 3 months post-discharge, disability was significantly higher in the SE group (p = 0.006); however, by 6 months, both groups showed comparable recovery (p = 0.345).
- ***Conclusions:*** Decreased consciousness, motor weakness, and supratentorial hemorrhagic lesions on MRI are significant predictors of SE in CVT patients. SE is associated with increased disability at 3 months, but long-term outcomes at 6 months are favorable in both SE and non-SE groups.
- **Keywords:** Cerebral venous thrombosis, Status epilepticus, Outcome

INTRODUCTION

Cerebral venous thrombosis (CVT), involving thrombosis of the dural sinuses and/or cerebral veins, is a relatively rare condition that primarily affects individuals under the age of 50. Women constitute approximately 75% of all CVT cases (1). Seizures are common, occurring in about one-third of adults and nearly half of children with CVT. Factors associated with seizure development include venous infarction, hemorrhagic transformation, and intracranial hypertension (2).

Accurate diagnosis requires a high index of clinical suspicion along with neuroimaging. Magnetic resonance imaging (MRI) combined with magnetic resonance venography (MRV) is the recommended imaging modality for diagnosing CVT (3). Contrast-enhanced MRV has greater sensitivity in detecting thrombi in smaller veins (4). Conventional angiography is generally reserved for cases in which the diagnosis remains uncertain after non-invasive imaging (5).

Identified risk factors for CVT include female sex, oral contraceptive use, pregnancy, the puerperium, and hormone replacement therapy (6). Transient predisposing factors include infections of the central nervous system or adjacent structures (ear, sinus, mouth, face), exposure to certain medications, head trauma, and invasive procedures such as lumbar puncture or jugular vein catheterization (6). Chronic risk factors include inherited or acquired thrombophilias (6).

The mainstay of CVT treatment is anticoagulation therapy (7). For patients with provoked CVT, warfarin (target INR 2.0–3.0) is typically administered for 3 to 6 months. In cases of unprovoked CVT, the duration of warfarin treatment may be extended to 6 to 12 months. Patients with recurrent CVT, venous thromboembolism following CVT, or those with severe thrombophilia may require indefinite anticoagulation (3). Overall, the prognosis of CVT is generally favorable (8).

PATIENT and METHOD

This comparative case series study was conducted at the Neurology Department of Al-Yarmouk Teaching Hospital and included all patients diagnosed with cerebral venous thrombosis (CVT) who were admitted between January 2019 and March 2021. Patients were categorized into three groups based on their initial presentation: those with status epilepticus (SE), those with epileptic seizures, and those without any seizure activity.

Clinical data were collected through direct patient interviews or extracted from medical records. The onset of CVT symptoms was classified as acute if hospitalization occurred

within 2 days, subacute if between 3 and 30 days, and chronic if more than 30 days had passed since symptom onset [9]. Status epilepticus was defined as either continuous seizure activity or two or more seizures without regaining consciousness for a duration exceeding 30 minutes. Epileptic seizure was defined as a transient occurrence of signs or symptoms due to abnormal, excessive, or synchronous neuronal activity in the brain [10]. Seizures or SE were further classified as acute symptomatic if they occurred within the first 7 days of initial CVT symptoms, or as remote symptomatic if they occurred after this period [11].

The study recorded demographic characteristics, duration from symptom onset, presence of headache, seizure, and focal neurological deficits. Glasgow Coma Scale (GCS) scores on admission were documented. Risk factors, along with MRI/MRV findings of the brain, were noted for all patients. Laboratory investigations included complete blood count, hemoglobin, coagulation profile, erythrocyte sedimentation rate, serum chemistry, HIV serology, chest radiograph, and electrocardiogram. Prothrombotic states were assessed by evaluating protein C, protein S, and antithrombin III levels, as well as screening for factor V Leiden mutation, antinuclear antibody, anti-dsDNA, antiphospholipid antibody, and lupus anticoagulant.

Upon confirmation of CVT diagnosis, all patients were treated with low-molecular-weight heparin (enoxaparin, 100 units/kg subcutaneously twice daily). Warfarin was introduced after 5–15 days of heparin with a target INR of 2.0 to 3.0. Antiepileptic drugs (AEDs) were administered to patients who developed seizures or SE; no prophylactic AEDs were given to those without seizures. In cases of raised intracranial pressure, acetazolamide and/or mannitol was prescribed. Once clinical improvement was observed, patients were discharged with regular INR monitoring every 21 days and were scheduled for follow-up visits at 3 and 6 months.

In-hospital mortality and its causes were recorded. At 3 and 6 months post-discharge, patients were re-evaluated, and outcomes were assessed using the modified Rankin Scale (mRS). Outcomes were classified as poor (mRS >2) or good recovery (mRS ≤2) [12].

Data were analyzed using SPSS version 27. Descriptive statistics such as frequency, percentage, mean, standard deviation, and range (minimum–maximum) were used. The Pearson Chi-square test (χ^2) was applied to assess differences in categorical data, with Yates' correction or Fisher's Exact Test used when applicable. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 29 patients were included in the study, with a marked female predominance—27 females and only 2 males. The age of participants ranged from 16 to 61 years, with a mean age of 31.3 ± 10.4 years. The mean duration from symptom onset to hospitalization was 10.3 ± 6.7 days. Among the study population, 11 patients (37.9%) developed status epilepticus

(SE), 10 patients (34.4%) experienced epileptic seizures without SE, and 8 patients (27.5%) had no seizures. The number of seizures per patient ranged from 1 to 5.

When comparing the SE group with those who did not develop SE, there were no significant differences in demographics or baseline risk factors. However, the SE group had a significantly lower Glasgow Coma Scale (GCS) score on admission ($p = 0.0001$), and motor weakness was significantly more common in this group ($p = 0.002$). Furthermore, the presence of supratentorial parenchymal brain lesions on imaging was independently associated with the development of SE ($p = 0.018$). SE occurred more frequently in patients with hemorrhagic infarctions, with a statistically significant association ($p = 0.003$).

While the mortality rate did not differ significantly between the SE and non-SE groups, disability at 3 months post-discharge, as assessed by the modified Rankin Scale (mRS), was significantly higher among patients with SE ($p = 0.003$). By 6 months, however, the difference in disability between the two groups was no longer statistically significant ($p = 0.236$).

Table 1. comparison between status epilepticus group and without status epilepticus group

		Status epilepticus		Without SE		P value
		No	%	No	%	
Age (years)	<20years	1	9.1	1	5.6	0.923
	20---29	5	45.5	9	50.0	
	30---39	3	27.3	6	33.3	
	=>40years	2	18.2	2	11.1	
	Mean±SD (Range)	31.9±11.6 (17-61)		30.9±9.9 (16-61)		
Gender	Male	-	-	2	11.1	0.252
	Female	11	100	16	88.9	
Headache	Present	11	100	18	100	-
	Absent	-	-	-	-	
Duration of illness (days)	Acute (<3)	2	18.2	1	5.6	0.427
	Subacute (3-30)	9	81.8	16	88.8	
	Chronic (>30)	-	-	1	5.6	
	Mean±SD (Range)	7.4±4.1 (2-14)		12.2±7.6 (2-35)		
Type of lesion	Hemorrhagic infarction	7	63.6	2	11.1	0.003*
	Infarction	4	36.4	7	38.9	
	No parenchymal lesion	-	-	9	50.0	
Risk factor	OCP	8	72.7	12	66.7	0.821
	Puerperium	2	18.2	2	11.1	
	Dehydration	1	9.1	2	11.1	
	Anemia	-	-	1	5.6	
	SLE	-	-	1	5.6	
Death at hospital	Dead	1	9.1	-	-	0.193
	Alive	10	90.9	18	100	
MRS at 3 months	0	-	-	12	66.7	0.003*
	1	4	40.0	4	22.2	
	2	4	40.0	-	-	
	3	2	20.0	1	5.6	
	4	-	-	1	5.6	
MRS at 6 months	0	8	80.0	17	94.4	0.236
	1	2	20.0	1	5.6	
Papilledema	Present	8	72.7	12	66.7	0.732
	Absent	3	27.3	6	33.3	
The 6th Cranial nerve palsy	Bilateral	8	72.7	7	38.9	0.121
	Unilateral	3	27.3	7	38.9	
	No palsy	-	-	4	22.2	
Motor deficit	Yes	11	100	8	44.4	0.002*
	No	-	-	10	55.6	
Glasgow Coma Scale	≤8	11	100	3	16.7	0.0001*
	>8	-	-	15	83.3	
	5	5	45.5	-	-	
	6	3	27.3	-	-	
Glasgow Coma Scale	7	3	27.3	1	5.6	
	8	-	-	2	11.1	
	10	-	-	1	5.6	
	11	-	-	1	5.6	
	13	-	-	2	11.1	
	14	-	-	2	11.1	
	15	-	-	9	50.0	
MRI Supratentorial Parenchymal Lesion	Yes	11	100	11	61.1	0.018*
	No	-	-	7	38.9	
Number of sinus involved	Single	8	72.7	17	94.4	0.100
	Multiple	3	27.3	1	5.6	
Superior Sagittal Sinus	Yes	7	63.6	9	50.0	0.474
	No	4	36.4	9	50.0	
Transverse sinus	Bilateral	-	-	1	5.6	0.418
	Right	6	54.5	5	27.8	
	Left	1	9.1	1	5.6	
	No	4	36.4	11	61.1	
Others	Yes	-	-	4	22.2	
	No	11	100	14	77.8	
Others	Cortical vein	-		1		
	Deep venous	-		1		
	Right sigmoid	-		2		

DISCUSSION

In this study, status epilepticus (SE) occurred in 37.9% of patients, while 34.4% experienced epileptic seizures, and 27.5% had no seizures. These findings contrast with the study by Kalita et al., who reported that among 90 patients with CVT, 42 had seizures, and only 11% developed SE (13). Similarly, Anandure et al. reported the incidence of generalized seizures in 65% of CVT patients, focal seizures in 25%, and focal seizures with secondary generalization in 10% (14).

In our study, 55% of seizures were acute symptomatic, while 45% were classified as remote, a proportion higher than that reported by Mahale et al., who found that 46% of CVT patients experienced acute seizures (15).

Gender distribution in this study showed a significant female predominance, with females comprising 93.1% of cases. This finding differs from Sha et al., who reported a female proportion of 55% (16), and Patil et al., who found 58% of their patients were female in a study of 50 CVT cases (17).

The age of patients in this study ranged from 16 to 61 years, with a mean age of 31.3 ± 10.4 years, which is in line with international data. For instance, Nasr et al. reported a mean age of 38.1 years in a multicenter study involving 11,400 CVT patients (18), and Haghighi et al. observed a mean age of 29.52 ± 34.8 years among 465 Iranian patients (19).

Headache was the most common presenting symptom, occurring in all patients. This aligns with findings by Agostoni et al. and Gunes et al., who reported headache as the most frequent manifestation of CVT, observed in 80–90% of cases (20, 21).

Papilledema was present in most patients across all groups in this study, consistent with Wasay et al., who reported it in 28–67.5% of CVT patients (22). Additionally, Ferro et al. found papilledema to be more frequent in patients with chronic onset or delayed presentation (23), and Coutinho et al. noted its higher prevalence in patients with cortical hemorrhage compared to those without (44% vs. 9%) (24).

Motor weakness was reported in 65.5% of patients, especially in those with SE or seizures, indicating a potential risk factor for SE development (25). This observation is supported by Ferro et al., who found that early symptomatic seizures were particularly common in patients with motor deficits (26).

Supratentorial brain lesions, especially hemorrhagic infarctions, were found to be strong predictors for both seizures and SE. This agrees with Masuhr et al., who reported that early intracranial hemorrhage and infarction were independent predictors of early epileptic seizures, particularly in patients with focal motor deficits, cortical vein thrombosis, and intracranial hemorrhage (25). Similarly, Ferro et al. highlighted that early symptomatic

seizures were more frequent in patients with motor deficits, focal edema, ischemic infarcts, or hemorrhage (26).

The superior sagittal sinus (SSS) was the most commonly affected site, seen in 63.6% of SE patients and 50% of seizure patients. Davoudi et al. demonstrated that the supratentorial region was the only CNS location independently associated with seizure development in CVT, supporting the significant role of SSS involvement (27).

Oral contraceptive pills (OCPs) were the most common risk factor identified, particularly among female patients, which is in agreement with Amoozegar et al., who confirmed that OCP use significantly increases the risk of CVT in women of reproductive age (28). However, Beier et al. found no evidence that exogenous sex hormones increase seizure risk in young adults without epilepsy (29).

In this study, mortality was recorded in one patient (3.4%) who belonged to the SE group and died due to refractory SE requiring ICU admission. Ferro et al. identified several risk factors for mortality in CVT, including age over 37, male sex, coma, mental status disturbances, hemorrhage on CT, deep venous thrombosis, CNS infections, and cancer (26).

Disability assessed at 3 months post-discharge was significantly higher among patients with SE, but by 6 months, all patients in the study had achieved a good recovery, with modified Rankin Scale scores below 2. This finding is consistent with the observations of Mehvari et al., who reported no long-term association between seizures and disability in CVT patients (30).

CONCLUSION

Status epilepticus was observed in more than one-third of patients diagnosed with cerebral venous thrombosis (CVT). The development of SE was significantly associated with specific clinical and radiological risk factors, including a decreased level of consciousness on admission, the presence of motor weakness, and supratentorial brain lesions on MRI—particularly those involving hemorrhagic infarctions. Despite its initial impact, the occurrence of SE did not significantly influence long-term mortality or disability in patients who received appropriate treatment and follow-up care.

Ethical Clearance:

Ethical approval was obtained from the scientific and ethical committee of the Iraqi Board for Medical Specialization, and verbal informed consent was secured from all participants after explaining the study's aims and ensuring data confidentiality.

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Conflicts of interest:
There are no conflicts of interest.

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