Epileptic Seizure development in Participants with Cerebral Venous Sinuses Thrombosis

Emad Hazim Mhmood

Ibn Sina Hospital, DOH of Ninwa, Ministry of health/ Environment, Mosul, Iraq

Corresponding author:

Mosul, Iraq

09647505216437

yaalaalbairmany@gmail.com

Conflict of Interest

The author declares that they have no competing interests.

Funding

None

ABSTRACT

Background: *Cerebral venous sinuses thrombosis (CVST) is a condition with multi etiology, can complicate to epileptic seizure. The study aimed to determine the incidence of seizure and to estimate the exaggerating factors in participants with CVST.*

Methods: *An observational case-control study enrolled 30 participants with CVST. Data including age, gender, clinical features and focal neurologic signs were collected. Patients were followed up for one year from initial diagnosis to the recognize of epileptic seizure.*

Results:*The mean age of patients was 35.2±14.2 years. Females were represented 70%, whereas males were 30% of the patients. The duration of symptoms of CVST was 9.6±5.5 days with an average hospital admission of 8.4±6.1 days. The most frequent symptom was headache which documented in 47(94%) of patients. Regarding MRI brain findings, hemorrhagic lesions found in 32%, and infarction in 68%. The superior sagittal and lateral sinuses were the most sinuses involved. The changes on MRI includingpunctiform foci in 72%,extensive edematous in 50%, the ventricle dilation in 56%,about 48% of CVST presented in acute phase, 40% in subacute phase and 12% in chronic phase, the majority of foci sized less than 0.5 mm (33, 66%), and the clot appeared hyperintense on T1 MRI in 60%, hyperintense on T2 MRI in 22%, whereas FLAIR picture seen in 18%.There were (5, 10%) patients had only focal seizures, (10, 20%) experienced generalized seizures, and (5, 10%) suffered mix of both. There were no significant differences between CVST patients with and without seizures in terms of age,*

gender, duration of symptoms, symptoms, and hospitalization. MRI imaging findings, neither hemorrhagic lesion nor infarction showed a significant association with the presence of seizure.

Conclusion: *Iraqi people are at high risk to develop CVST. There are several signals in CVST patients to development of seizure as MRI findings, and occlusion site of sinuses. Awareness need to be rise and the monitoring must be undertake about the risk factors for the development of seizure in CVST patients.*

Keywords: *Cerebral venous sinuses thrombosis; Epileptic seizure; Hemorrhage; Infarction;Superior sagittal sinus*

Introduction

Cerebral venous sinuses thrombosis (CVST) is a rare disease of cerebrovascular net can effect young adult [1]. It is responsible for only 0.5–1% of all strokes [2]. Recognized risk factors for it comprise pregnancy or puerperium, using oral contraceptive pills (CCP), and coagulopathy disorders, therefore, the most affected peoples are woman [1]. Clinically, headache, vomiting, focal neurological deficits, and various degrees of disturbance in consciousness level as well as mental dysfunction are the main symptoms. Furthermore, epileptic seizures are a common and important clinical features, accounting in about 1/3 of population affected by CVST [3]. Previously, it reported as a first sign in 29% of the CVST patients, with about 60% of these cases presenting with seizure [4]. On the other hand, frequent epileptic seizures were recognized as important risk factors for short-term death in these patients [5, 6]. In particular, the seizures are important to determine the survival in CVST patients. Only few studies have addressed the factors correlated with the development of epileptic seizures in CVST patients [7, 8]. Estimating these factors assistant the neurosurgeons to decide the proper management and, therefore reducing the possible harm of epilepsy [8].

Here, this study aimed to evaluate the risk factors for developing epileptic seizures in a sample of patients with CVST.

Materials and Methods

Study design and setting

An observational case-control study was conducted at Ibn Sina Hospital, Mosul, Iraq. The study included a total of 50 patients who were admitted to this center with CVST from June 2020 to May 2021. The diagnosis was based on the clinical features, signs of increased intracranial pressure and focal

neurological manifestation. In addition, magnetic resonance imaging (MRI) accompanied with venography was used to confirm the diagnosis of CVST.

Participants

CNS infection, head trauma, those planned for surgical management for CVST, those receiving anticoagulant treatment for an indication other than CVST (requiring continuation of the treatment), severe renal impairment, active liver disease, pregnancy, nursing or planning to become pregnant were excluded from this study.

Data Collection

Data were collected according to the standardized questioner sheet: age, gender, clinical features, including fever, headache, vomiting, consciousness level and focal neurologic signs (weakness and motor or sensory signs). Imaging findings included hemorrhage, infarction foci (location and sizes), the shape of foci, presence of edema, ventricle dilation, phase of CVST, and the clot appearance. Others data including duration of symptoms, and hospitalization.

Intervention

All participants had received subcutaneous low molecular weight heparin (0.1 mL/10 kg/ 1 per 12h) for two weeks, and oral warfarin (dose was set based on the international normalized ratio (INR 2–3)) thereafter. The follow-up period was six month-period assigning the patients during which the development of epileptic seizure was recognized.

Data Analysis

Descriptive statistics 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 of Fisher's exact test for categorical variables. A significant difference was set at $p<0.05$. All analyses were conducted with SPSS V.25.0 (Chicago, USA).

Results

The mean age of patients of this study was 35.2±14.2 years. Females were represented 70%, whereas males were 30% of the patients. The duration of symptoms of CVST was 9.6±5.5 days with an average hospital admission of 8.4±6.1 days. The most frequent symptom was headache which documented in 47(94%) of patients, followed by altered consciousness (Confusion, fainting, and coma) in 66%, blurred of vision in 30%, motor signs (Loss of control over movement in part of the body) in 28%, and sensory signs in 24%. Regarding MRI brain findings, hemorrhagic lesions found in 32%, and infarction in 68%.

The superior sagittal and lateral sinuses were the most sinuses involved in (35, 70%), whereas the intracranial sinus was the least involved (11, 22%). (Table 1)

Table 1: Demographic andclinical characteristics ofpatients with CVST.

Variables		No.(%) / mean±SD
Age (years)		35.2±14.3
Gender	Male	15 (30)
	Female	35 (70)
Duration ofsymptoms (days)		9.6±5.5
Hospitalization (days)		8.4±6.1
Symptoms	Headache	47 (94)
	Altered consciousness	33 (66)
	Blurred vision	15 (30)
	Motor signs	14 (28)
	Sensory signs	12 (24)
MRI brain findings	Hemorrhage	16 (32)
	Infarction	34 (68)
Sinus thrombosis	Superior sagittal	35 (70)
	Lateral	35 (70)
	Intracranial	11 (22)

Table 2 showed the changes on MRI, according to the shape, punctiform foci found in 72% and sheet-like in 26%. Extensive edematous lesions are seen in 50%, partial edema in 30% and lesions without edema in 20%. The ventricle dilation documented in 56% of MRI. About 48% of CVST presented in acute phase, 40% in subacute phase and 12% in chronic phase. Almost, the majority of foci sized less than 0.5 mm (33, 66%), while 17(34%) of lesions sized more than or equal to 0.5 mm. The clot appeared hyperintense on T1 MRI in 60%, hyperintense on T2 MRI in 22%, whereas FLAIR picture seen in 18%.

Table 2: MRI changes inpatients with CVST.

Variables		No.(%) / mean±SD
Finding	Punctiform	36 (72)

shape	Sheet-like	13 (26)
	Other (irregular)	1 (2)
Edema	Extensive	25 (50)
	Partial	15 (30)
	No	10 (20)
Ventricle dilation	Present	28 (56)
	Not present	22 (44)
Phase	Acute	24 (48)
	Subacute	20 (40)
	Chronic	6 (12)
Size (mm)	<0.5	33 (66)
	≥0.5	17 (34)
Appearance	Hyperintenseon T1	30 (60)
	Hyperintense on T2	11 (22)
	FLAIR	9 (18)

Regarding seizure type that developed during follow-up in this study, there were (5, 10%) patients had only focal seizures, (10, 20%) experienced generalized seizures, and (5, 10%) suffered mix of both. There were no significant differences between CVST patients with and without seizures in terms of age, gender, duration of symptoms, symptoms, and hospitalization. MRI imaging findings, neither hemorrhagic lesion nor infarction showed a significant association with the presence of seizure. The superior sagittal sinus thrombosis was observed in 17(34%) patients without seizure, while 18(36%%) of patients without seizures were recognized to have the involvement of superior sinus. In addition, lateral and intracranial sinus thrombosis were not of a significant association weather CVTS patients have seizure or not. (Table 3)

Table 3: Correlation between variables of CVST.

Variables		Without seizure (No.= 30)	Focal seizure (No.=5)	Generalized seizure (No.=10)	Mixed seizure (No.=5)	p-value
		No.(%) / mean±SD				
Age (years)		34.3±12.2	36.7±15.2	36.5±14.8	38.1±12.7	0.12
Gender	**Male (No.=15)**	7 (14)	1 (2)	5 (10)	2 (4)	0.5
	Female (No.=35)	23 (46)	4 (8)	5 (10)	3 (6)	0.1
Duration ofsymptoms (days)		8.9±3.6	8.1±5.8	9±4.6	8.2±6.1	0.2
Hospitalization (days)		7.8±6.1	7.2±5.5	7.4±4.3	6.9±5.7	0.2
Symptoms	**Headache**	30 (60)	5 (10)	8 (16)	4 (8)	0.08
	Altered consciousness	13 (26)	5 (10)	10 (20)	5 (10)	0.06
	Blurred vision	5 (10)	3 (6)	3 (6)	4 (8)	0.2
	Motor signs	4 (8)	3 (6)	3 (6)	4 (8)	0.2
	Sensory signs	3 (6)	3 (6)	3 (6)	3 (6)	1
MRI brain findings	**Hemorrhage**	7 (14)	3 (6)	3 (6)	3 (6)	0.1
	Infarction	3 (6)	2 (4)	7 (14)	3 (3)	0.15
Sinus thrombosis	**Superior sagittal**	17 (34)	5 (10)	9 (18)	4 (8)	0.07
	Lateral	20 (40)	3 (6)	8 (16)	4 (8)	0.4
	Intracranial	1 (2)	1 (2)	4 (8)	5 (10)	0.6

Discussion

This study faced and confirmed 30 cases of CVST during one year. This maybe reflect a high incidence of CVST compared with previous studies Qatar and Turkey [1, 9].

In general, the mean age in this study was 35.2±14.3 years, yet this in consistent with most previous studies like [8, 10-12], but several studies reported even younger ages maybe develop CVST. Nasr et al., in an international study on more than 11 thousands patient with CVST documented a mean age of 38.1 years [10], whereas Haghighi et al., in Iran, recorded that the mean age was 29.52±34.8 years in confirmed CVST patients [13]. In this study, women were more affected by CVST than men (M:F ratio was 1:2), which is agree with most previous studies [8, 11, 13, 14].The most common symptoms observed was headache which may be associated with altered consciousness. Furthermore, there is

almost a general consensus among several studies that the headache is the most common symptom in CVST [13].

Hemorrhage, and infarction, were documented as the main findings in MRI. Similarly, several studies showed the same results like [7, 14].

Superior sagittal sinus thrombosis was the most sinus affected in 70%, the same was shown by Stam et al., [12]. Gunes et al., [1], and Anadure et al., [15] recorded that the transverse sinus was the most sinus occluded. This could be explained by that these two sinuses is involved due to their normal function as a major dural sinuses which receive seem to be a large amount of venous drainage [16].

Here, 30(60%) of patients were not recorded epilepsy in the follow-up. While 20(40%) patients had developed seizure within same period of follow-up. In india, a review study by Patil et al., [11] reported that 21(42%) of CVST patients had developed seizures. In addition, Sha et al., [8] revealed that 32(46.38%) patients had experienced a secondary seizure. These variations in percent may be altered by several conditions as age of patients, marital status, parity, drugs, comorbid diseases, inflammatory diseases and infections [14-17].

In general, focal seizure documented in 10%, generalized seizure in 20% and mixed of both in 10% of patients. These findings were small in comparison with Ding et al., study [7], they recorded generalized seizure in 69.21%, focal in 13.5% and focal with secondary generalized in 11.5%. Also, the same was reported by Anadure et al., study [15], they said that the incidence of generalized, focal and focal plus secondary generalized seizure in were 65%, 25% and 10%, respectively.

Whenever compared between patients without seizure and those that developed seizure among age of patients, gender, duration of disease, hospital period, symptoms of disease, MRI findings, and sinus thrombosis site, there were no significant differences. This is disagree with Ding et al., [7], they found that confusion, was significantly related to CVST patients that developed seizure in comparison with those people without seizure. Also, disagree with Bano et al., [18], which recently published a prospective cross-sectional analysis from a Tertiary care hospital in Pakistan. Patil et al., [11] revealed that the involvement of sinuses were mostly frequently correlated with the development of seizure in CVST.

Conclusion

Iraqi people are at high risk to develop CVST. There are several signals in CVST patients to development of seizure as MRI findings, and occlusion site of sinuses. Awareness need to be rise and

the monitoring must be undertake about the risk factors for the development of seizure in CVST patients.

Acknowledgments

The author is grateful to Dr. Ahmed Salih Alshewered to his help.

Ethical Clearance

This study was approved by Ibn Sina Hospital, DOH of Ninwa.

References

1. Gunes HN, Cokal BG, Guler SK, et al. Clinical associations, biological risk factors and outcomes of cerebral venous sinus thrombosis. *J Int Med Res*. 2016;44(6):1454-1461. doi:10.1177/0300060516664807
2. Stam J. Thrombosis of the cerebral veins and sinuses. *N Engl J Med*. 2005;352(17):1791-1798. doi:10.1056/NEJMra042354
3. Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F; ISCVT Investigators. Early seizures in cerebral vein and dural sinus thrombosis: risk factors and role of antiepileptics. *Stroke*. 2008;39(4):1152-1158. doi:10.1161/STROKEAHA.107.487363
4. Sidhom Y, Mansour M, Messelmani M, et al. Cerebral venous thrombosis: clinical features, risk factors, and long-term outcome in a Tunisian cohort. *J Stroke Cerebrovasc Dis*. 2014;23(6):1291-1295. doi:10.1016/j.jstrokecerebrovasdis.2013.10.025
5. Mahale R, Mehta A, John AA, et al. Acute seizures in cerebral venous sinus thrombosis: What predicts it?. *Epilepsy Res*. 2016;123:1-5. doi:10.1016/j.eplepsyres.2016.01.011
6. Zuurbier SM, Hiltunen S, Tatlisumak T, et al. Admission Hyperglycemia and Clinical Outcome in Cerebral Venous Thrombosis. *Stroke*. 2016;47(2):390-396. doi:10.1161/STROKEAHA.115.011177
7. Ding H, Xie Y, Li L, et al. Clinical features of seizures after cerebral venous sinus thrombosis and its effect on outcome among Chinese Han population. *Stroke Vasc Neurol*. 2017;2(4):184-188. Published 2017 Aug 27. doi:10.1136/svn-2017-000095
8. Sha DJ, Qian J, Gu SS, Wang LN, Wang F, Xu Y. Cerebral venous sinus thrombosis complicated by seizures: a retrospective analysis of 69 cases. *J Thromb Thrombolysis*. 2018;45(1):186-191. doi:10.1007/s11239-017-1570-5

9. Algherbawe MT, Khan FY, Abonof SS, et al. Clinical characteristics and outcome of cerebral venous sinus thrombosis: A 4-year Hospital- based study from 2008 to 2011. Libyan J Med Sci 2017;1:36-9.
10. Nasr DM, Brinjikji W, Cloft HJ, Saposnik G, Rabinstein AA. Mortality in cerebral venous thrombosis: results from the national inpatient sample database. *Cerebrovasc Dis*. 2013;35(1):40-44. doi:10.1159/000343653
11. Patil VC, Choraria K, Desai N, Agrawal S. Clinical profile and outcome of cerebral venous sinus thrombosis at tertiary care center. *J Neurosci Rural Pract*. 2014;5(3):218-224. doi:10.4103/0976-3147.133559
12. Stam J, Majoie CB, van Delden OM, van Lienden KP, Reekers JA. Endovascular thrombectomy and thrombolysis for severe cerebral sinus thrombosis: a prospective study. *Stroke*. 2008;39(5):1487-1490. doi:10.1161/STROKEAHA.107.502658
13. BorhaniHaghighi A, Ashjazadeh N, Safari A, Cruz-Flores S. Cerebral venous sinus thrombosis in iran: cumulative data, shortcomings and future directions. *Iran Red Crescent Med J*. 2012;14(12):805-810. doi:10.5812/ircmj.3728
14. Banakar BF, Hiregoudar V. Clinical Profile, Outcome, and Prognostic Factors of Cortical Venous Thrombosis in a Tertiary Care Hospital, India. *J Neurosci Rural Pract*. 2017;8(2):204-208. doi:10.4103/0976-3147.203812
15. Anadure RK, Wilson V, Sahu S, Singhal A, Kota S. A study of clinical, radiological and etiological profile of cerebral venous sinus thrombosis at a tertiary care center. *Med J Armed Forces India*. 2018;74(4):326-332. doi:10.1016/j.mjafi.2017.11.004
16. Liu Y, Li K, Huang Y, Sun J, Gao X. Treatment of the superior sagittal sinus and transverse sinus thrombosis associated with intracranial hemorrhage with the mechanical thrombectomy and thrombolytics: Case report. *Medicine (Baltimore)*. 2017;96(49):e9038. doi:10.1097/MD.0000000000009038
17. Amoozegar F, Ronksley PE, Sauve R, Menon BK. Hormonal contraceptives and cerebral venous thrombosis risk: a systematic review and meta-analysis. *Front Neurol*. 2015;6:7. Published 2015 Feb 2. doi:10.3389/fneur.2015.00007
18. Bano S, Farooq MU, Nazir S, et al. Structural Imaging Characteristic, Clinical Features and Risk Factors of Cerebral Venous Sinus Thrombosis: A Prospective Cross-Sectional Analysis from a

Tertiary Care Hospital in Pakistan. *Diagnostics (Basel)*. 2021;11(6):958. Published 2021 May 26. doi:10.3390/diagnostics11060958