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Original Research Article

Study of factors affecting hospital outcome of cerebral venous thrombosis

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Abstract

Background: Cerebral venous thrombosis (CVT) is condition characterized by thrombosis of intracranial veins and sinus which results in parenchymal damage and rise in intracranial pressure. The present research was undertaken to study the factors affecting hospital outcome of CVT.
Method: Total 100 patients presented with clinical features of CVT proved on CT or MRI venography admitted in wards or ICCU of tertiary care centre during the period from November 2016 to October 2018, were included in the study.At the time of admission various clinical, radiological and laboratorial factors were evaluated to find out relationship with hospital outcome (recovery or mortality) in CVT patients.
Results: Risk factors like alcoholism, smoking, and PNC status had insignificant association ($P > 0.05$) while hypertension showed significant association with ($P < 0.05$) hospital outcome. Among clinical predictors, neurological focal deficit and seizures had insignificant association ($P > 0.05$) while Glassgow coma scale score at admission showed significant association ($P < 0.05$). Among laboratory predictors, admission hyperglycemia and anaemia (≤ 9gm/dl) had significant association ($P < 0.05$) while D-dimer had insignificant association ($P > 0.05$) with hospital outcome. Among radiological predictors, haemorrhagic transformation and number of sinuses involved did not showed significant ($P > 0.05$) association with hospital outcome in patients with CVT. The mortality rate was found to be 10%.
Conclusion: CVT even with a reduced occurrence represents a severe neurovascular emergency. Better control of blood glucose levels will be needed and anaemia should be corrected as soon as is diagnosed to improve the hospital outcome in patients with CVT.
Keywords: Cerebral venous thrombosis, Risk factors, Outcome, Seizure, Hyperglycemia, Anaemia, Mortality.

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1. Introduction

Cerebral venous/sinus thrombosis (CVT) has been recognized in the early part of the nineteenth century but still remains a diagnostic and therapeutic challenge for the clinician because of varying and misleading clinical presentation of this condition. It forms a distinct subgroup of cerebrovascular disease in India [1] and is a leading cause of mortality in women of reproductive age group [2]. In India, most of the cases are seen in post-partum period in women, while alcoholism is a significant risk factor in males. Review of CVT cases from Asian countries is suggestive of differences in risk factors profile and outcome in these patients as compared to European studies [3].

The diagnosis of cerebral venous/sinus thrombosis requires high index of suspicion [4]. With the advent of imaging modalities like CT scan and recently Magnetic Resonance Imaging (MRI) and Magnetic resonance venography (MRV), the diagnosis of CVT has improved significantly. CT scan commonly shows haemorrhagic infarctions with or without “cord”, or “empty delta” sign [5]. It may be normal in 10% of patients [6]. In such cases advanced neurological diagnostic like magnetic resonance imaging with venography is necessary to confirm cerebral venous thrombosis, but it is not always readily available in many hospitals. MRI and MRV, when used in doubtful situations can clarify the diagnosis by showing thrombosed sinus of cortical veins [7]. In fact after the introduction of

MRV, many of the patients earlier diagnosed as Idiopathic raised ICT have been noted to have sinus thrombosis giving rise to syndrome of raised intracranial pressure without localization.

Pathologically involvement of superior sagittal sinus of varying extent with or without the involvement of transverse and sigmoid sinuses with thrombosis of cortical veins had been reported commonly [6]. Haemorrhagic infarctions with mass effect and diffused cerebral edema with herniation is also frequently seen. Involvement of deep venous system is less common than superficial venous system but by no means rare. Due to multifactorial causation of this condition, it will be interesting to know whether different factors at the time of admission will have different effect on the outcome. Short term outcome of CVT in this part of the state is not well described, so the present study was undertaken to study the factors affecting hospital outcome of patients with cerebral venous thrombosis.

2. Materials and Methods

After obtaining Institutional Ethics Committee approval and written inform consent from each patient, this hospital based cross sectional observational study was conducted in 100 patients, who were presented with clinical features of CVT proved on CT or MRI venography admitted in wards or ICCU of tertiary care centre during the period of 2 years from November 2016 to October 2018. Patients who denied consent, patients presenting with clinical features of CVT but not confirmed on CT venography or MRI venography and patients with previous history of CVT were excluded from the study.

A detailed history was taken, general examination, CNS, CVS, respiration system and per-abdomen examination and all relevant laboratory investigations were done. Clinical diagnosis was confirmed by CT or MRI venography in all patients. At the time of admission various clinical, radiological and laboratorical factors were evaluated like Admission hyperglycemia, Anaemia, Seizures, D-dimer levels, GCS grading, Hemorrhagic transformation, focal Neurological deficit, Number of sinuses involved to find out relationship of these factors with hospital outcome (recovery or mortality) in cerebral venous thrombosis patients.

2.1 Statistical Analysis

Data was entered in Microsoft Excel and were analysed using SPSS version 21.0(statistical package for the social sciences, Armonk, NY, USA). The main outcomes for analysis were the number and proportion of patients with CVT for the outcome of health. Bivariate analysis was performed to find the association of various factors and health outcome of patients. An odd ratio (ORs) with 95% Cis was used to describe associations between groups. Multivariate analysis using conditional logistic regression was performed to calculate adjusted ORs. In all analyses, P values less than 0.05 were considered significant.

3. Observations and Results

Total 100 patients were enrolled in the study among them 68 (68%) were males and 32 (32%) were females. The majority of patients (41%) were from the age group of 21 -30 years followed by 21% from the age group of 31-40 years, (Table 1). The mean age of patients was 33.68±13.26 years.

Table 1: Age and Gender Distribution of Patients

Age group (years)	Gender		Total (%)
	Male (%)	Female (%)	
11-20	07 (10.3)	06 (18.8)	13 (13)
21-30	29 (42.6)	12 (37.5)	41 (41)
31-40	15 (22.1)	06 (18.8)	21 (21)
41-50	06 (8.8)	04 (12.5)	10 (10)
≥51	11 (16.2)	04 (12.5)	15 (15)
Total	68 (100)	32 (100)	100 (100)

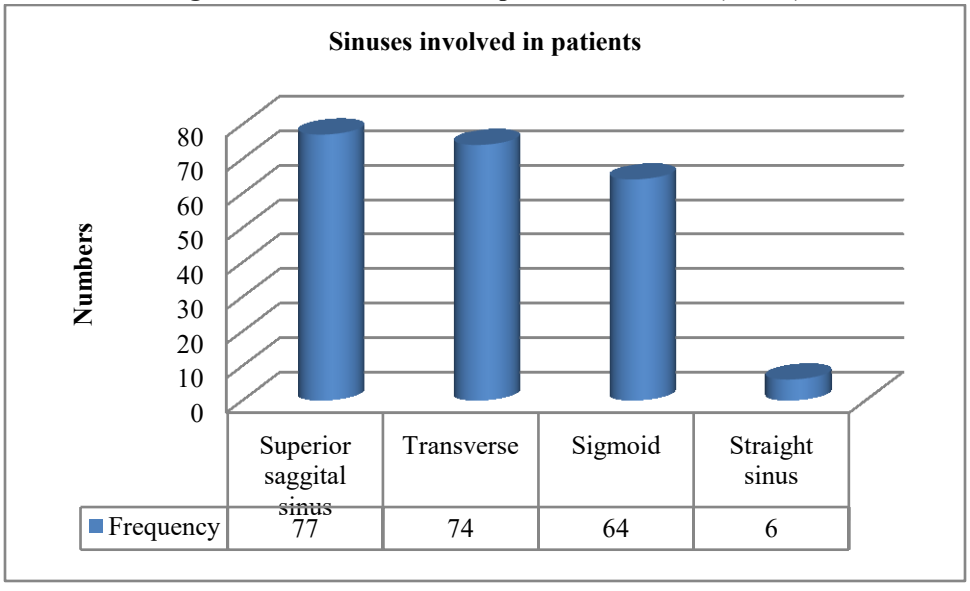
At the time of admission various clinical, laboratorial and radiological factors were evaluated as shown in table 2. Most common presenting complaint was headache present in 89 (89 %) patients. Altered sensorium found in 50 % of patients and it was categorised according to Glasgow coma scale (GCS) shown in table 2.41% patients presented with seizures and seizures were categorised in the form of partial and generalised tonic clonic seizures. 26% patients presented with neurological focal deficit (Hemiparesis, hemiplegia, aphasia and cranial nerve involvement).

Table 2: Predictors of Poor Hospital Outcome in CVT at the time of admission

Predictors			Frequency	Percentage
Clinical predictors	Focal Neurological deficit		26	26
	Seizure		41	41
	Glasgow Coma Scale	GCS score 13-15	50	50
		GCS score 9-12	40	40
		GCS score ≤ 8	10	10
Lab predictors	Hyperglycemia (≥ 141 mg/dl)		44	44
	Anaemia (≤ 9 gm/dl)		29	29
	Raised D-dimer		21	215
Radiological predictors found on CT venography	Haemorrhagic transformation		53	53
	Sinuses involved	>2	51	51
		≤ 2	49	49

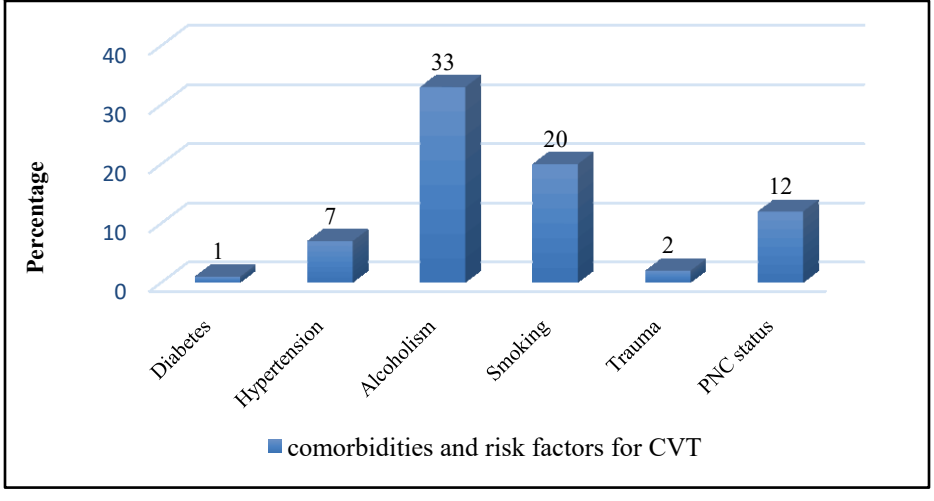
One sinus was involved in 23 patients. Two sinuses were involved in 26 patients. Multiple sinuses were involved in 51 patients. Most common sinus involved was superior saggital sinuses 77 % followed by trasverse sinus (74 %) as shown in figure 1. Few patients have involvement of inferior sagittal sinus. In current study not a single patients have involvement of lateral sinus.

Figure 1: Sinuses involved in patients with CVT (n=100)



In co-morbidities, hypertension was present in 7 (7%) patients and diabetes mellitus was present in 1 patient. In risk factors, history of alcohol addiction was found in 33(33%) patients and smoking in 20(20%) patients. Past History of trauma to head was found in 2 patients. PNC status was found in 12 patients, (Figure 2).

Figure 2: Co-morbidities and Risk factors in patients with cerebral venous thrombosis



Out of 100 patients, 90 patients recovered (60 males and 30 females) and 10 patients died. Thus, mortality was found to be 10 %. Out of 10 patients died, 08 were males and 02 were females. Age > 40 years has significant association with hospital outcome in cerebral venous thrombosis. (P=0.00, ORs=0.063, 95% CI= 0.012-O.320). There was no significant association between gender and hospital outcome in patients with CVT. (P=0.391, ORs=0.500, 95% CI=0.100-2.502), (Table 3).

Alcoholism, smoking, PNC status had insignificant association (P > 0.05) while hypertension showed significant association with (P < 0.05) hospital outcome. Among clinical predictors, neurological focal deficit and seizures did not show significant association (P> 0.05) while Glassgow coma scale score at admission have significant association (P < 0.05) with hospital outcome. Among laboratory predictors, admission hyperglycemia and anaemia (≤ 9gm/dl) had significant association (P <0.05) while D-dimer had insignificant association (P>0.05) with hospital outcome. Among radiological predictors, haemorrhagic transformation and number of sinuses involved did not showed significant (P >0.05) association with hospital outcome in patients of CVT, (Table 3).

Table 3: Association of Independent variable with hospital outcome in patients of cerebral venous thrombosis- Univariate analysis

Independent variable		Hospital Outcome		Total (%)	Odds ratio (95% CI)	P value
		Died (%)	Recovered (%)			
Age group (Years)	≤40	2 (2.7)	72 (97.3)	74 (100)	0.063(0.012-0.320)	0.00
	>40	8 (30.8)	18(69.2)	26 (100)		
Gender	Female	2(6.2)	30 (93.8)	32 (100)	0.500(0.100-2.502)	0.391
	Male	8(11.8)	60 (88.2)	68 (100)		
Hypertension	No	6(6.5)	87 (93.5)	93 (100)	0.05(0.009-0.286)	0.00
	Yes	4(57.1)	3 (42.9)	7 (100)		
Alcoholism	No	5(7.5)	62(92.5)	67 (100)	0.452(0.121-1.686)	0.228
	Yes	5 (15.2)	28(84.8)	33 (100)		
Smoking	No	10 (12.5)	70 (87.5)	80 (100)	0.875 (0.805-0.951)	0.096
	Yes	0 (00)	20 (100)	20 (100)		
PNC Status	No	10 (11.4)	78 (88.6)	88 (100)	0.886 (0.822-0.955)	0.218
	Yes	0 (00)	12(100)	12 (100)		
Seizure	No	5 (8.5)	54 (91.5)	59 (100)	0.667 (0.180-2.469)	0.542
	Yes	5 (12.2)	36 (87.8)	41 (100)		
Focal Neuro-logical deficit	No	04 (5.4)	70 (94.6)	74 (100)	0.190(0.049-0.742)	0.010
	Yes	6(23.1)	20 (76.9)	26 (100)		
Glasgow Coma Scale	GCS 13-15	0(00)	43(100)	43(100)	-	0.000
	GCS 9-12	2(5.3)	36(94.7)	38(100)		
	GCS ≤ 8	8(42.1)	11(57.9)	19(100)		
Admission Hyperglycemia	No	0 (0)	56 (100)	56 (100)	1.294(1.103-1.519)	0.00
	Yes	10 (22.7)	34 (77.3)	44 (100)		
Anaemia	No	3 (4.2)	68 (95.8)	71 (100)	0.139 (0.033-0.583)	0.003
	Yes	7 (24.1)	22 (75.9)	29 (100)		
D-dimer	Raised	1 (4.8)	20 (95.2)	21 (100)	2.571 (0.307-21.528)	0.368
	Normal	9 (11.4)	70(88.6)	79 (100)		
Haemorrhagic transformation	No	1 (2.1)	46(97.9)	47 (100)	0.106 (0.013-0.874)	0.013
	Yes	9 (17)	44(83)	53 (100)		
Sinuses involved	≤2	3 (6.1)	46 (93.9)	49 (100)	0.410 (0.100-1.686)	0.205
	>2	7(13.7)	44 (86.3)	51 (100)		

The factors which have significant association with hospital outcome in patients of CVT independently were again analysed by multivariate analysis to find their association with hospital outcome in combination by removing confounding factors. By multivariate analysis, admission hyperglycemia and anaemia (≤ 9 gm/dl) had significant association with hospital outcome while age >40, haemorrhagic transformation and focal Neurological deficit had insignificant association with hospital outcome in patients with CVT, (Table 4).

Table 4: Multivariate adjusted analysis of significant factors for predicting hospital outcome in patients with CVT

Significant Factors		Odds ratio (95% CI)	P value
Age	>40	0.17 (0.02-1.06)	0.05
	≤40	Ref	
Admission hyperglycemia	Yes	0.14(0.02-0.98)	0.04
	No	Ref	
Anaemia	Yes	0.21 (0.39-1.14)	0.03
	No	Ref	
Haemorrhagic transformation	Yes	0.24 (0.22-2.71)	0.25
	No	Ref	
Focal Neurological deficit	Yes	0.71 (1.13-3.83)	0.69
	No	Ref	

4. Discussion

The present study shows mean age of presentation in cerebral venous thrombosis from 20 to 46 years which was in concordance with the previous studies [8-11]. But age > 40 years did not showed significant association with hospital outcome in patients with CVT, this not in correlation with above studies [8-11] probably because of small sample size of present study. The male preponderance observed in the study with male to female ratio of 2:1, this finding was correlated with the study done by Narayan *et al* [11]. The maximum number of males in current study may be because of more consumption of alcohol and smoking in males and better obstetric care and higher level of clinical suspicion and detection of cerebral venous thrombosis at an early age in female. Most common presenting complaint was headache followed by altered sensorium, seizures and neurological focal deficit, this result was correlated with other studies [12-14].

4.1 Risk factors

Diabetes mellitus was present in 1 patient, hypertension in 7 patients, alcoholism in 33 patients, smoking in 20 patients, trauma in 2 patients and PNC status in 12 patients. Among hypertensive patients (7 patients), 4(57.1%) patients were died and 3(42.9%) recovered. 93 patients were without hypertension out of which 6(6.5%) died while 87(93.5%) recovered. Thus, hypertension showed significant association with hospital outcome in patients with CVT ($P < 0.05$); this was correlated with the study done by Narayan *et al* [11]. Out of 33 alcoholic patients 5(15.2%) died and 28(84.8%) recovered. 67 patients were non-alcoholics of which 5(7.5%) died and 62(92.5%) patients recovered. 20 patients were smokers of which all (100%) recovered and 80 patients were non-smokers of which 10(12.5%) patients died. 12 patients were having PNC status of which all(100%) patients recovered. 88 patients were without PNC status of 10(11.4%) died and 78(88.6%) patients recovered. Thus alcoholism, smoking, PNC status had insignificant association with hospital outcome in patients with CVT ($P > 0.05$).

4.2 Clinical predictors

Out of 100, 41 patients presented with seizures of which 5 died and rest of all recovered. Thus seizures did not showed significant association with hospital outcome ($P > 0.05$), which was correlated with the earlier studies [12, 15-18].26 patients presented with focal neurological deficit of which 6 patients died and 20 patients' recovered and 74 patients were without focal neurological deficit of which 4 patients died. Thus focal neurological deficit did not showed significant association with hospital outcome. Focal Neurological deficit increases the hospital stay and morbidity in patients with CVT but is not directly related to hospital outcome (death) of the patients. Also due to early diagnosis and improved treatment guidelines, there is good and early recovery in patients of CVT. 43 patients had a GCS score 13-15 of which all (100%) patients recovered. 38 patients had GCS score 9-12 of which 2(5.3%) patients died and 36(94.7%) patients' recovered. 19 patients had GCS score ≤ 8 of which 8(42.5%) patients died and 11(57.9%) patients recovered. Thus there was significant association between GCS score at admission and hospital outcome in patients with CVT, ($P < 0.05$) and this findings were compared with the other studies[12, 19].

The multivariate analysis was not applied on risk factors and GCS score due to small sample size of current study.

4.3 Laboratory predictors

44 patients out of 100 presented with admission hyperglycemia of which 10 patients died and 56 patients were without hyperglycemia out of which all patients recovered. 29 patients presented with anaemia of which 7 (24.1%) died and 71 patients were without anaemia of which 3 (4.2%) died. Thus both the admission hyperglycemia and anaemia found significant association with hospital outcome. This result was compared with the previous studies [20-22]. Many researchers blamed thrombocytosis for venous thromboembolism as iron deficiency anaemia causes secondary thrombocytosis. Previously it was known that anaemia is a risk factor for CVT but present study showed that it affects the hospital outcome in patients with CVT. D-dimer was raised in 21 patients out of which 1(4.8%) patient died and 79 patients were with normal D-dimer of which 9(11.4%) patients died. Thus it showed no significant association between D-dimer and hospital outcome, ($P > 0.05$).Low risk patients were defined as headache patients with a normal neurological examination, normal standard head CT and absence of risk factors such as pregnancy or puerperium. Normal D-dimers in these patients may reduce unnecessary imaging, making it a potential valuable marker. Thus D-dimer is a predictor of CVT which can be used as a tool for screening of patients with headache to rule out CVT which can avoid unnecessary imaging. It does not have any association with hospital outcome in patients with CVT.

4.4 Radiological predictors

53 patients presented with haemorrhagic transformation of which 9(17%) patients died and 44(83%) patients recovered. 47 patients presented without haemorrhagic transformation of which only 1 patient died and 46 patients recovered. Thus haemorrhagic transformation did not showed significant association with hospital outcome ($P > 0.05$). These findings were not in correlation with the previous studies [12,19, 23], this is because previously there was delay in diagnosis and treatment of cerebral venous thrombosis which led to unfavourable outcome. But in present era, mortality rate was decreased due to better imaging studies and improved health care; there is improved outcome in patients of CVT. Cerebral venous thrombosis even with a reduced occurrence represents a severe neurovascular emergency. The number of sinuses involved does not affect the hospital outcome of patient.

5. Conclusion

The present study revealed significant number of patients affected by cerebral venous thrombosis in 3rd and 4th decade of life, predominantly affecting male population. Risk factors like Alcoholism, smoking are being increasingly identified, while conventional risk factors like postpartum are decreasing. Admission hyperglycemia and anaemia are independent predictors of health outcome while GCS grading (low score) at the time of admission also predicts poor hospital outcome in patients with CVT. Better control of blood glucose levels will be needed and anaemia should be corrected as soon as is diagnosed to improve the hospital outcome in patients of CVT patients. The mortality rate was found to be 10%; these contradictory findings were due to early diagnosis due to better imaging facilities and improved health care facilities in present era.

Small sample size was the only limitation of this study. However, prospective study with large cohort will be needed to confirm present results.

References

[1]. 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):218-24.

[2]. Nagaraja D, Sarma G. Treatment of cerebral sinus/venous thrombosis. *Neurology India*. 2002; 50(2):114-6.

[3]. Cantu C, Barinagarrementeria F. Cerebral venous thrombosis associated with pregnancy and puerperium. Review of 67 cases. *Stroke*. 1993; 24(12):1880-85.

[4]. Sohoni CA. Acute cerebral venous sinus thrombosis: A rare complication of binge drinking. *J Sci Soc.* 2014; 41(3):192-4.

[5]. Virapongse C, Cazenave C, Quisling R, Sarwar M, Hunter S. The empty delta sign: frequency and significance in 76 cases of dural sinus thrombosis. *Radiology*. 1987; 162(3):779-85.

[6]. Bousser MG, Chiras J, Bones J, Castaigne P. Cerebral venous thrombosis. A review of 38 cases. *Stroke.* 1985; 16(2):199-213.

[7]. Bansal BC, Gupta RR, Prakash C. Stroke during pregnancy and puerperium in young females below the age of 40 years as a result of cerebral venous/venous sinus thrombosis. *Japanese Heart Journal.* 1980; 21(2):171-83.

[8]. Coutinho JM, Zuurbier SM, Aramideh M, Stam J. The incidence of cerebral venous thrombosis: a cross-sectional study. *Stroke.* 2012; 43(12):3375-7.

[9]. Gunes HN, Cokal BG, Guler SK, Yoldas TK, Malkan UY, Demircan CS, *et al*. Clinical associations, biological risk factors and outcomes of cerebral venous sinus thrombosis. *Journal of International Medical Research.* 2016;44(6):1454-61

[10]. Patil VC, Choraria K, Desai N, Agrawal S. Clinical profile and outcome of cerebral venous sinus thrombosis at tertiary care center. *Journal of Neurosciences in Rural Practice.* 2014; 5(3):218-24.

[11]. Narayan D, Kaul S, Ravishankar K, Suryaprabha T, Bandaru VC, Mridula KR, *et al*. Risk factors, clinical profile, and long-term outcome of 428 patients of cerebral sinus venous thrombosis: insights from Nizam's Institute Venous Stroke Registry, Hyderabad (India). *Neurology India*. 2012; 60(2):154-9.

[12]. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F, Investigators I. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke.* 2004; 35(3):664-70.

[13]. Sassi SB, Touati N, Baccouche H, Drissi C, Romdhane NB, Hentati F. Cerebral Venous Thrombosis: A Tunisian Monocenter Study on 160 Patients. *Clinical and applied Thrombosis/Hemostasis* 2017; 23(8):1005-9.

[14]. Barboza MA, Chiquete E, Arauz A, Merlos-Benitez M, Quiroz-Compeán A, Barinagarrementería F, *et al*. A Practical Score for Prediction of Outcome after Cerebral Venous Thrombosis. *Frontiers in Neurology*. 2018; 9:882-8.

[15]. Stolz E, Valdueza JM, Grebe M, Schlachetzki F, Schmitt E, Madlener K, *et al*. Anemia as a risk factor for cerebral venous thrombosis? An old hypothesis revisited. *Journal of Neurology*. 2007; 254(6):729.

[16]. Mehvari Habibabadi J, Saadatnia M, Tabrizi N. Seizure in cerebral venous and sinus thrombosis. *Epilepsia Open.* 2018; 3(3):316-22.

[17]. Mahale R, Mehta A, John AA, Buddaraju K, Shankar AK, Javali M, *et al*. Acute seizures in cerebral venous sinus thrombosis: What predicts it? *Epilepsy Research*. 2016; 123:1-5.

[18]. Korathanakhun P, Sathirapanya P, Geater SL, Petpichetchian W. Predictors of Hospital Outcome in Patients with Cerebral Venous Thrombosis. *Journal of Stroke and Cerebrovascular Diseases*. 2014; 23(10): 2725-9.

[19]. deBruijn SF, de Haan RJ, Stam J. Clinical features and prognostic factors of cerebral venous sinus thrombosis in a prospective series of 59 patients. For The Cerebral Venous Sinus Thrombosis Study Group. *Journal of Neurology, Neurosurgery, and Psychiatry.* 2001; 70(1):105-8.

[20]. Zuurbier Susanna M, Hiltunen S, Tatlisumak T, Peters Guusje M, Silvis Suzanne M, Haapaniemi E, *et al*. Admission Hyperglycemia and Clinical Outcome in Cerebral Venous Thrombosis. *Stroke*. 2016; 47(2): 390-6.

[21]. Yong M, Kaste M. Dynamic of hyperglycemia as a predictor of stroke outcome in the ECASS-II trial. *Stroke.* 2008; 39(10):2749-55.

[22]. Coutinho Jonathan M, Zuurbier Susanna M, GaartmanAafke E, Dikstaal Arienne A, Stam J, Middeldorp S, *et al*. Association Between Anemia and Cerebral Venous Thrombosis. *Stroke.* 2015; 46(10):2735-40.

[23]. Wingerchuk DM, Wijdicks EF, Fulgham JR. Cerebral venous thrombosis complicated by hemorrhagic infarction: factors affecting the initiation and safety of anticoagulation. *Cerebrovascular Diseases (Basel, Switzerland)*. 1998; 8(1):25-8.