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ALCOHOL : A PROVOCATING FACTOR IN MALE CEREBRAL VENOUS THROMBOSIS – A PROSPECTIVE ANALYSIS IN WESTERN RAJASTHAN

Neurology

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ABSTRACT

BACKGROUND : Cerebral venous thrombosis is an uncommon cause of headache in our daily practice. However there is a need to identify its various provoking factors because timely and appropriate therapy can reverse the disease process , its acute complications and long term sequel.
OBJECTIVE : To study the clinical profile in male Cerebral Venous Thrombosis patients .
METHODS AND MATERIAL : This is a prospective cross sectional study of twenty five male Cerebral Venous Thrombosis (CVT) patients diagnosed in outpatient clinic of neurology department at Dr S N medical college from the September , 2014 to august , 2018. Their ages ranged from 10 to 70 years with mean age of onset 31 yrs. All patients after taking informed consent with history suggestive of CVT and later diagnosed by imaging of brain (MRI and MRV) were included.
STATISTICAL ANALYSIS USED: All data were expressed as mean or patient's number (n) and percentage (%) as appropriate
RESULTS: Among 25 male CVT patients , majority were young seen in 20-30yrs with mean age of 31yrs. Most common clinical presentation was headache [n=25(100%)] with or without vomiting followed by seizures [n=10 (40%)]. Most common site involved was transverse sinus [n=23(92%)]. Papilledema was observe in 21 patients (84%). Alcoholism [n=8 (32%)] and hyperhomocystenemia [n=6(24%)] were the risk factors seen in male CVT.
CONCLUSION: Cerebral Venous Thrombois is found to be significantly high in alcoholic males. Compared to other Indian studies there was not much disparity in clinical profile and risk factors.

KEYWORDS

Papilledema, Cerebral Venous Thrombosis, alcoholism

INTRODUCTION:

Cerebral Venous Thrombosis (CVT) is a rare form of cerebrovascular disease with variable manifestations like headache , focal neurological deficit, seizure and altered sensorium [1] thus making the diagnosis difficult. [2] Indian studies revealed that CVT contribute to 10% of all stroke.[3] Earlier studies from India showed an increase incidence of CVT in women (Dash 2015) [4] due to puerperium, Oral contraceptive pills and hormone replacement therapy. However recent studies (Pai 2013,[5] Narayan 2012 [6])showed that males are equally or more affected by CVT compared to females. Hereditary and acquired prothrombotic conditions are a major risk factor in male CVT. Among males , alcoholism is a major cause to predispose CVT by causing a state of dehydration , hyperviscosity , increased platelet reactivity leading to an acquired prothrombotic state . Thus a high index of suspicion is needed to make a diagnosis and prevent further complications.

MATERIALS AND METHODS:

Twenty five male patients diagnosed to have CVT and proven by MRI were selected after taking informed written consent and ethical approval from outpatient clinic of neurology department at Dr S N medical college from the period from September , 2014 to August , 2018. Their ages ranged from 10 to 70 years . Detailed history was taken with respect to clinical features, substance abuse and alcohol addiction . All patients were subjected to detailed neurological and systemic examination for any evidence of anemia, dehydration, DVT of leg . Etiological work up was done to identify the cause and risk factors like malignancy, systemic disease, hyperhomocystenemia ,prothrombotic conditions. Genetic studies for mutations were, however not done due to economic limitations. Hyperhomocysteinemia was defined as serum homocysteine level more than 15mg/100ml in less than 60 year old patients and more than 20mg/100 ml in more than 60 year old patients.[7,8] Anemia was defined as hemoglobin level of less than 13gm/dl in men and 12gm/ dl in women as per World Health Organisation (WHO) guidelines.[9] MRI and MRV was done in all patients. Patients with indefinite evidence of CVT on imaging and presence of hypertensive haemorrhage , arterial stroke , metabolic encephalopathy and presence of space occupying lesions on imaging are excluded.

Statistical Analysis:

The data were collected. P-value less than 0.05 was considered statistically significant. All data were expressed as mean or patient's number (n) and percentage (%) as appropriate.

RESULTS:

Twenty five male CVT patients were diagnosed and included in our study. Their ages ranged from 10 to 70 years with mean age of onset 31 yrs. Majority were in 20-30s age group [Fig 1] The most common clinical presentation was headache seen in all patients (100%) with vomiting in 24 (96%) patients. Majority had a sub acute onset of symptoms [n=14,(56%)] , acute in [n=4(16%)] and chronic in [n=7(28%)] .

Seizures was observed in 40% (n=10) of the patients. Focal seizures with secondarily generalisation was the most common semiology observed in [n=7 (70%)]. 3 patients had Generalised Tonic Clonic Seizures. Motor weakness was observed in 5 patients (20%) and all had hemiparesis. 4 patients had altered sensorium at the time of presentation. Papilledema was observed in 21 patients (84%) out of which majority had grade 4 degree of papilledema (44%). Fever was absent in all. Cranial Nerve involvement was noted in 16%. Most common cranial nerve affected was unilateral sixth Nerve (8%) and facial (8%) nerve. Addictions were observed in 10 patients (40%) out of which [n=8 (80%) were chronic alcoholics. [n=2(20%)] of the patients were addicted to cigarette smoking / tobacco chewing. All Alcoholics in our study were heavy drinkers. Mild Anaemia was observed in 20% of the patients All patients had venous sinus thrombosis in MR venography. Many patients had multiple venous sinus involvement and transverse sinus was noted to be the most common sinus involved [n=23 (92%)] followed by Superior sagittal sinus [n=20(80%)] . The major risk factors identified were alcoholism [n=8(32%)], hyperhomocystenemia [n=6(24%)], Factor V mutation, behcet disease, malignancy, dehydration all contributed equally to 4%. No specific etiological diagnosis could be found in majority of the patients[n=5 (20%)]. All patients were treated with anticoagulants and followed up to six months. 3 left against medical advice. 2 died and rest became asymptomatic. Clinical Profile and venous system involvement of CVST is summarised in Table 1 and Fig 2 respectively.

Fig 1.

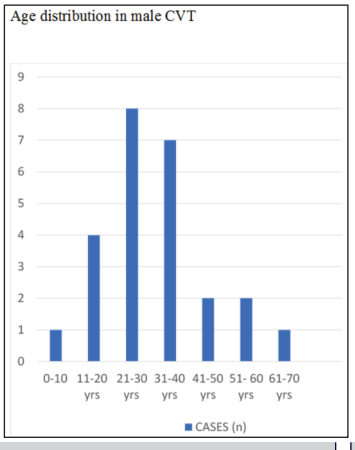
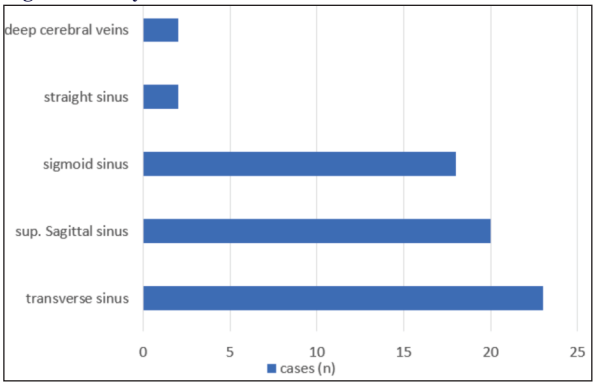


Table 1 Clinical profile of male CVT patients

Parameters	No of cases (%)
Sample size	25
Mean age (yrs)	31yrs
Age range (yrs)	10-70
Onset	
1. Acute	4 (16%)
2. Sub acute	14 (56%)
3. Chronic	7 (28%)
Symptoms and signs	
1. Headache	25 (100%)
2. Vomiting	24 (96%)
3. Seizures	10 (40%)
a. GTCS b. Focal	3 (30 %) 7 (70%)
4. Weakness a. Hemiparesis	5 (20 %) 5 (20%)
5. Altered sensorium	4(16 %)
6. Fever	0
7. Crania nerve palsy	4 (16 %)
8. papilloedema	21(84%)
9. diplopia	2 (8 %)
Risk factors	
Hyperhomocystenemia	6 (24 %)
Alcohol	8(32 %)
Anemia	5 (20%)
infection	0
Fa V (leiden) mutation	1 (4%)
Malignancy	1 (4%)
Behcet	1 (4 %)
Polycythemia	2 (8%)
Dehydration	1 (4 %)
idiopathic	5 (20 %)
Drug abuse	0 (0 %)
Protein s deficiency	0
Protein c deficiency	0

Fig. 2 Venous system involvement in CVT



DISCUSSION:

Cerebral venous thrombosis is a diagnostic challenge for clinicians because of variable pattern of presentation. Many studies has been done on puerperal CVT . Recently the scenario of CVT is changing . Modern imaging technique like MRI and MRV and good obstetric care has led to decreased incidence of CVT in females . Nowadays there is a male dominance seen by various Indian studies (Narayan et al (2012) [6], Pai et al (2013) [5]) . Although various Indian and western studies have been done on CVT [Table 2], a systematic study was lacking from western India ,Rajasthan. Hence a study was conducted focusing on predisposing factors of CVT in males.

In our study , majority had CVT in 20-30s age group . Mean age is 31 yrs. In comparison ,the mean age was 31 yrs in study by Narayan et al [6] whereas in western studies ICVST [10] the mean age is 39yrs. Headache was most common and early detected symptom in our study

Headache with or without vomiting was found in 100% patients. The possible hypothesis explained was stretching of the nerve fibres in the walls of the occluded sinus and local inflammation as suggested by the evidence of contrast enhancement of the sinus wall surrounding the clot. [11]

Headache was most commonly sub acute in onset in [n=14 (56%)] ,acute in [n=4 (16%)] , and chronic in [n=7 (28%)] patients. Stroke like presentation was seen in 20%[n= 5] patients in which all had hemiparesis. Encephalopathy was seen in 16 %[n=4].. Cranial nerve involvement seen in [n= 4(16%)] Seizures occurred in [n=10 (40%)]. 70 %(n=7) had focal seizures and 30%(n=3) had generalized seizures. In a study by Narayan et al (2012) [6], Pai et al (2013)[5] , seizures was the most common symptom followed by stroke while in Ferro *et al*. (2004) [10] , most common symptom was headache followed by seizures similar to our study. In our study, Papilloedema was seen in [n=21 (84%)] patients in which Grade IV papilloedema was most common sign contributing to 44% (n= 11). This is high which may be due to delayed presentation of most cases. On MRV , most common sinus involved was transverse sinus [n= 23(92%)], followed by superior sagittal sinus[n= 20(80%)]. In contrast , Narayan et al (2012), Pai et al (2013), Ferro et al (2004) found superior sagittal sinus involvement was most common followed by transverse sinus. In our study , the predisposing risk factors observed in males were alcoholism [n= 8(32%)], hyperhomocystenemia [n=6 (24%)], mild anemia [n=5 (20%)], dehydration [n= 1(4%)], protein c and s deficiency [n= 0(0%)], behcet disease [n=1 (4%)], polycythemia vera [n=2 (8%)], factor V mutation [n= 1(4%)], malignancy [n=1 (4%)] and idiopathic in[n=5(20%)]. All alcoholics were chronic heavy drinkers. In our study , alcoholism and hyperhomocystenemia were the most common risk factors found in men. Narayan et al found that anemia and alcoholism were most common risk factors and among prothrombotic conditions , hyperhomocystenemia followed by protein S deficiency. Heavy alcohol consumption may be an independent risk factor for endothelial dysfunction.[12] through the nitric oxide (NO) pathway. There is an interference with NO production or release from endothelial cells by chronic alcohol consumption [13]; especially, high concentrations of alcohol reduce NO synthesis and endothelial proliferation. [14]

Furthermore, high concentrations of ethanol activates the proapoptotic caspase pathway. [15] Thus heavy alcohol consumption causes higher procoagulant state and an impaired fibrinolytic potential,[16,17] activities which can predispose individuals to thrombosis.[18,19] Acute ingestion of large but tolerable dose of alcohol transiently increases thromboxane-mediated platelet activation,[20] and hyperagreegation is observed after acute alcohol consumption. [21] Moreover, long-term alcohol causes chronic liver damage causing a state of overall decreased synthesis of anticoagulant thrombotic factors.[22] Virchow triad(triad of Stasis, hypercoagulability, and endothelial dysfunction) is believed to contribute to thrombosis.[23] Our study emphasized that increase consumption of alcohol has led to high incidence of CVT in males and most of the alcoholics presented with raised intracranial pressure . Thus whenever heavy alcoholics present with raised intracranial pressure , CVT must be excluded. All patients were treated with anticoagulants and followed up to six months. 3 left against medical advice. One died and the outcome was favourable in rest of them.

Table 2 : Comparison between series of patients with cerebral venous thrombosis

	INDIAN STUDIES				WESTERN STUDIES	
Series	**Narayan et al. 2012**	**Pai et al. 2013**	**Aneesh et al 2017**	**Jeyaram et al 2019**	**Wassay et al. 2008**	**Ferro et al 2004**
Study design	retrospective	retrospective	Ambispective	prospective	ambispective	prospective
Sample size	428	612	116	203(all males)	182	624
Mean Age (μ = yrs)	31.3yrs	31.9 yrs	35.21 yrs	38 +6.9yrs	38yrs	39.1yrs
Age range (yrs)	8-65yrs	-------	21-30 yrs.	--------	13-42 yrs	16-86 yrs
Sex ratio (M/F)	1.16:1	3:2	1.3:1	All males	2:5	1:4
MC symptom	Seizures > paresis	Headache > paresis	Men (Sz> Headache) Females (headache> vomiting)	Headache > seizures	Headache > paresis	Headache > seizures

Risk factor	Anemia= hyperhomocysteinemia> alcohol	Infection > Genetic thrombophilia	Males (Alcohol) Females (puerperium>OCP)	Alcohol> cigarette	Genetic thrombophilia	OCPs> Genetic thrombophilia
MC sinus involved	Sup. Sagittal sinus> transverse sinus	Sup. Sagittal sinus > cortical venous thrombosis	Sup. Sagittal sinus> transverse sinus	Sup. Sagittal sinus> transverse sinus	Sup. Sagittal sinus	Sup. Sagittal sinus> transverse sinus

CONCLUSION

CVT is uncommon but treatable disesase. Alcoholism is strongly associated with male CVT . Prognosis is good if treated early. High index of suspicion of CVT is indicated if chronic alcoholic presenting with headache with raised intracranial pressure.

REFERENCES

1. Poon CS, Chang JK, Swarnkar A, et al. Radiologic diagnosis of cerebral venous thrombosis: pictorial review. Am J Radiol 2007;189: S64–S75.
2. Karthikeyan D, Vijay S, Kumar T, et al. Cerebral venous thrombosis-spectrum of CT findings. Neuroradiology 2004;14:129- 37.
3. Banerjee AK., Varma M., Vasista RK., Chopra JS. 1989.Cerebrovascular disease in north-west India: a study of necropsy material. *J Neurol Neurosurg Psychiatry*. pr;52(4):512–5.
4. Dash D., Prasad K., Joseph L. 2015. Cerebral venous thrombosis: An Indian perspective. *Neurol India*. Jun;63(3):318–28.
5. Pai N., Ghosh K., Shetty S. 2013. Hereditary thrombophilia in cerebral venous thrombosis: a study from India. *Blood Coagul Fibrinolysis Int J Haemost Thromb*. Jul;24(5):540–3.
6. Narayan D., Kaul S., Ravishankar K., Suryaprabha T., Bandaru VCSS., Mridula KR. *et al*., 2012. 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). Neurol India. Apr;60(2):154–9.
7. Ueland PM, Refsum H, Stabler SP, Malinow R, Andersson A, Allen RH. Total homocysteine in plasma or serum: Methods and clinical applications. Clin Chem 1993;39:1764 -79.
8. Clarke R, Woodhouse P, Ulvik A, Frost C, Sherlikar P, Refsum H, et al. Variability and determinants of total homocysteine concentrationin plasma in an elderly population. Clin Chem 1998;44:102-7.
9. Harrison's Principles of Internal Medicine. Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson L, Loscalzo J. (Editors), 19th edition, 2015, McGraw Hill Education, United States of America.
10. Ferro JM., Canhão P., Stam J., Bousser MG., Barinagarrementeria F. 2004. ISCVT Investigators.
11. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke. Mar;35(3):664– 70
12. Tanaka A, Cui R, Kitamura A, et al. Heavy alcohol consumption is associated with impaired endothelial function. J Atheroscler Thromb 2016;23:1047–54.
13. Puddey IB, Zilkens RR, Croft KD, et al. Alcohol and endothelial function: a brief review. Clin Exp Pharmacol Physiol 2001;28:1020–4.
14. Kuhlmann CR, Li F, Ludders DW, et al. Dose-dependent activation of Ca2+-activated K+ channels by ethanol contributes to improved endothelial cell functions. Alcohol Clin Exp Res 2004;28:1005–11.
15. Liu J, Tian Z, Gao B, et al. Dose-dependent activation of antiapoptotic and proapoptotic pathways by ethanol treatment in human vascular endothelial cells: differential involvement of adenosine. J Biol Chem 2002;277:20927–33.
16. Lee KW, Lip GY. Effects of lifestyle on hemostasis, fibrinolysis, and platelet reactivity: a systematic review. Arch Intern Med 2003;163: 2368–92.
17. Mukamal KJ, Jadhav PP, D'Agostino RB, et al. Alcohol consumption and hemostatic factors: analysis of the Framingham Offspring cohort.Circulation 2001;104:1367–73.
18. Smith FB, Lee AJ, Fowkes FG, et al. Hemostatic factors as predictors of ischemic heart disease and stroke in the Edinburgh Artery Study. Arterioscler Thromb Vasc Biol 1997;17: 3321–5.
19. Ridker PM, Hennekens CH, Stampfer MJ, et al. Prospective study of endogenous tissue plasminogen activator and risk of stroke. Lancet1994;343:940–3.
20. Numminen H, Syrjala M, Benthin G, et al. The effect of acute ingestion of a large dose of alcohol on the hemostatic system and its circadian variation. Stroke 2000;31:1269–73.
21. Ruf JC. Wine and polyphenols related to platelet aggregation and atherothrombosis. Drugs Exp Clin Res 1999;25:125–31.
22. Aggarwal A, Puri K, Liangpunsakul S. Deep vein thrombosis and pulmonary embolism in cirrhotic patients: systematic review. World J Gastroenterol 2014;20:5737–45.
23. Wolberg AS, Aleman MM, Leiderman K, et al. Procoagulant activity in hemostasis and thrombosis: Virchow's triad revisited. Anesth Analg 2012;114:275–85.