

Association Of Central Venous Sinus Thrombosis With Vitamin B12 And Homocysteine Level

Dr Ajay Dabhi , Dr Divyeshwari Chauhan , Dr Pratishtha Shrivastav ,
Dr Nilam Gabani
2(Medicine , Government Medical College Vadodara , India)

Abstract:

Background: Cerebral venous sinus thrombosis (CVST) is an uncommon condition which over the past few years has been diagnosed more frequently due to greater awareness and the availability of better non-invasive diagnostic techniques. The main progress in CVT study has been focused on identification of thrombophilic factors. Epidemiological studies have suggested that even mild hyperhomocysteinemia (hyper-Hcy) is associated with occlusive arterial vascular disease and venous thromboembolism. Hyper-Hcy increases the risk of CVT by 4-fold. Conversely, because blood levels of folate, vitamin B12, and to a lesser extent vitamin B6, are related inversely to homocysteine, anyone with a nutritional deficiency of these vitamins is at increased risk of hyper-Hcy. In the present case-control study, a hypothesis was posed accordingly proposing hyper-Hcy as a risk factor for development of CVT in association with the MTHFR mutation or with a deficient nutritional status resulting from inadequate ingestion of vitamins such as Vitamin B12.

Materials and Methods: A cross sectional study was conducted in department of general medicine , SSG hospital baroda ,after obtaining informed consent,24 patients of >12 years. Patient were subjected to appropriate laboratory investigation such a serum Homocysteine Level of Serum B12 Level CT brain with angiogram, complete hemogram, blood urea, serum creatinine, liver function test other investigations if necessary

Results: Mean age of the patient was 28 years and majority of patients were females .Most common presentation was headache , followed by nausea vomiting and altered mental status . Maximum 64% of the patient had dehydration followed by infection 56%. Half of the females i.e, 50% of the females were pregnant and 32% had Hyperhomocysteinemia and 28% low vitamin b12 levels. shows Sagittal Sinus (48%) involvement as most common involvement

in Central venous sinus thrombosis followed by Sigmoid and/or Transverse sinus (28%).

Conclusion: Significant proportion of individual with CVST had Hyper homocysteinemia. Methyl cobalamine, folic acid, and pyridoxine supplements to the patient with Hyperhomocysteinemia will be helpful in the prevention of CVST.

Date of Submission: 08-05-2023

Date of Acceptance: 18-05-2023

I. Introduction

Diabetes is now commonly recognized as a coronary heart disease risk equivalent^{1,2,3,4}. This is mainly attributed to the high rates of dyslipidemia among diabetic patients which is believed to be one of the major factors accounting for the high percentage of deaths among diabetics due to cardiovascular disease (CVD)⁵. Numerous epidemiological studies and randomized controlled trials have documented the association between elevated LDL-C levels with increased CVD risk in both diabetic and non diabetic populations.^{6,7} Thus reducing LDL-C levels is the primary goal of therapy for diabetic dyslipidemia.^{5,8} Statins are considered the first pharmacological line of treatment of dyslipidemia in diabetic patients⁹. Lowering of LDL-C levels is thought to be the main beneficial effect of statin treatment. In India currently no guidelines available for treating diabetic dyslipidemia and no previous study has documented the efficacy. The current study aims to build growing awareness of atherosclerosis specific care of diabetes patient by examining efficacy of two most commonly prescribed statins in India.

II. Material And Methods

This Cross-Sectional Study was conducted during 2020 in Department of General Medicine at Baroda Medical College, Vadodara, India. After obtaining a fully informed written consent of 24 patient were enrolled in the study. Patients more than 12 years of age were enrolled in the study. Patient not given consent were excluded from this study. Patient will be subjected to appropriate laboratory investigation such a serum Homocysteine Level of Serum B12 Level CT brain with angiogram, complete hemogram, blood urea, serum creatinine, liver function test other investigations if necessary.

Study Design: Cross Sectional Study.

Sample Size: 25 patients were taken in the study.

Study Population: Patients admitted in SSG Hospital with Cerebral Venous Sinus Thrombosis.

Inclusion Criteria: Patient admitted in SSG with Cerebral Venous Sinus Thrombosis with age greater than 12 years

Exclusion Criteria: Patient not giving consent. Patient who are already and Vitamin B12 therapy

Data Collection: After taking written informed consent about enrollment in this study and maintaining adequate privacy and confidentiality, all the patient was subjected to standardize research protocol detailed history was taken in each case all patient meeting inclusion and exclusion criteria were selected thoroughly. Data Analysis: All data will be analyzed using Descriptive statistics (frequency, percentage,mean +SD), Chi Square test and specificity, sensitivity, positive prediction value and negative prediction value will be obtained.

III. Result

Mean age of the patient was 28 years and majority of patients were females .Most common presentation was headache , followed by nausea vomiting and altered mental status . Maximum 64% of the patient had dehydration followed by infection 56%. Half of the females i.e, 50% of the females were pregnant and 32% had Hyperhomocysteinemia and 28% low vitamin b12 levels. shows Sagittal Sinus (48%) involvement as most common involvement in Central venous sinus thrombosis followed by Sigmoid and/or Transverse sinus (28%).

Clinical Features	All patients (n=25)	Age		
		<40 yo	≥ 40 yo	P-value
Headache	81.5	95.6	78.6	0.08
Seizures	19.3	22.2	14.3	0.71
Nausea / Vomiting	47.6	60	50	0.51
Altered mental status	47.6	44.4	57.9	0.41
Focal motor deficit	16.9	15.6	21.4	0.69
Impaired speech	20.3	2.2	21.4	0.04

Table : Represents Symptoms according to age.

Total no. of Deaths	Mean age (years)	Mean age of Males	Mean age of Females (years)
Male Death (n=4)	48.87±12.6	58.5±9	39.25±11.5
Female Death (n=7)			

Table: Represents Mean age of death due to cerebral venous thrombosis.

IV. Discussion

CVST is reported to be more common in developing countries, and has been linked to pregnancy, multiparity, dehydration, and infection. Developments in imaging, diagnostic laboratory investigations, and genetics have provided valuable information about risk factors and clinical spectrum of CVST. We compared our experience of CVST, highlighting its diverse clinical presentations, predisposing factors, and neuroimaging with other studies from India and abroad. CVST represents 0.5%-1% of all strokes. According to the largest cohort study, 78% cases occurred in patients younger than 50 years. One pathological study found a prevalence of CVT of 9.3% among 182 consecutive autopsies. No population studies have reported the incidence of CVST.

Hyperhomocysteinemia is a risk factor for CSVT and stroke but has not been clearly associated with an increased risk of CVST. [1] Twenty-four percent of our population had Hyperhomocysteinemia and more

predominantly in female population. Lath et al. [5] stated that the mortality in CVST, in addition to progressive thrombosis, is related to elevated intracranial pressure causing transtentorial herniation. They reported a mortality of 27%. These findings are comparable with our result with a low mortality of 16%. Lath et al. reported that the decompressive surgery for patients with large cerebral venous infarcts is a life-saving procedure.

Similarly, in our study, 3 (6%) patients underwent decompressive surgery of whom 2 patients improved and 1 succumbed. Pfefferkorn et al. [4] studied 32 patients with CVST with headache (81%) being common presenting symptom. Out of 32 patients, 9 (28%) had deep cerebral venous system thrombosis (DCVST) and 23 (72%) had non-isolated DCVST.

Similarly, headache in 45 (90%) patients was the most common presenting feature in our study. Infection dehydration hyperhomocysteinemia and peripartum state were the important precipitating or risk factors, either individually or in combination for development of CVST in our study with mortality of 16%.

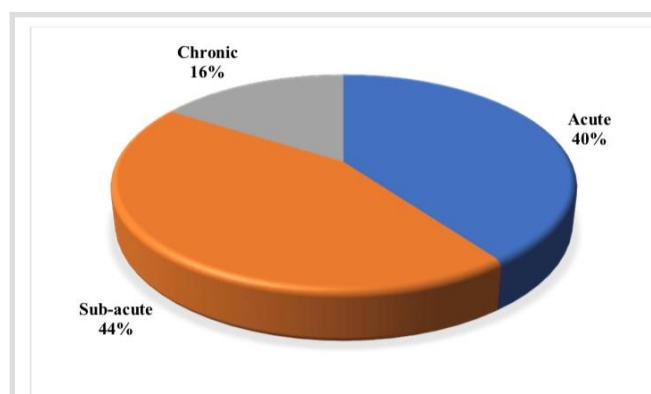


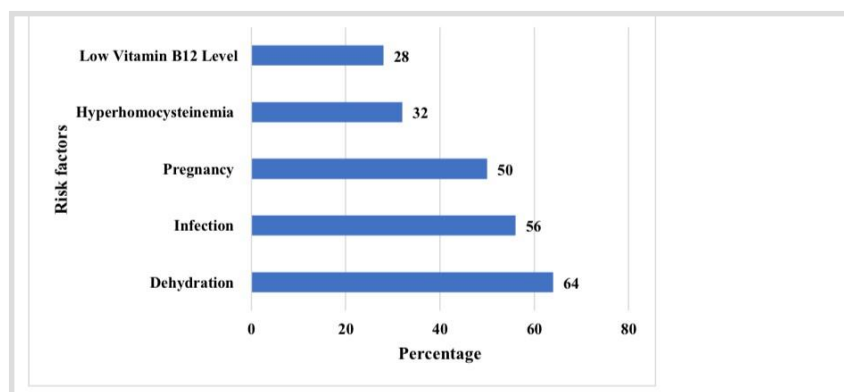
Figure: Modes of presentation of cerebral venous thrombosis.

Risk Factors*	Total	Percentage
Dehydration	16	64
Infection	14	56
Pregnancy	8	50 (n=16)
Hyperhomocysteinemia	8	32
Low Vitamin B12 Level	7	28

Table : Risk factors for cerebral venous thrombosis.

Sinuses	Deaths	Mean duration of stay
Sagittal	4	4.75 days
Sigmoid/transverse	3	1 day
Cavernous	0	0
Multiple sinuses	3	5.6 days

Table: cerebral venous sinus involvement, death, duration of stay.



V. Conclusion

The present study revealed significant number of patients affected by CVST in 2nd and 3rd decade of life, predominantly affecting female population, approximately one third. Most common sinus affected in male was sigmoid and transverse sinus thrombosis. Sagittal sinus was most commonly affected in female population. Affections of sigmoid, transverse, and multiple sinus thrombosis had more mortality and morbidity with longer duration of stay and residual significant neurodeficit. Headache and vomiting were the most common presenting symptoms and next was seizure.

Infection and dehydration are the common precipitating factors for development of CVST in developing countries, including India.

Prevention and proper management of infection and dehydration with supplementation of folic acid methyl cobalamin, and pyridoxine are mandatory for prevention and management of CVST along with LMWH, anticonvulsant, and decongestive drugs. Peripartum period is vulnerable for development of CVST due to the presence of infection and dehydration.

Methyl cobalamine, folic acid, and pyridoxine supplements to the patient with Hyperhomocysteinemia will be helpful in the prevention of CVST.

References

- [1]. Allroggen H, Abbott RJ. Cerebral venous sinus thrombosis. *Postgraduate Medical Journal*. 2000 Jan 1;76(891):12-5.
- [2]. Falcon CR, Cattaneo M, Panzeri D, Martinelli I, Mannucci PM. High prevalence of hyperhomocyst(e)inemia in patients with juvenile venous thrombosis. *Arterioscler Thromb Vasc Biol*. 1994;14:1080-1083.
- [3]. Den Heijer M, Blom HJ, Gerrits WBJ, Rosendaal FR, Haak HL. Is hyperhomocysteinaemia a risk factor for recurrent venous thrombosis? *Lancet*. 1995;345:882-885.
- [4]. Simioni P, Prandoni P, Burlina A, Tormene D, Sardella C, Ferrari V, Benedetti L, Girolani A. Hyperhomocysteinemia and deep-vein thrombosis: a case control study. *Thromb Haemost*. 1996;76:883-886.
- [5]. DenHeijerM, KosterT, BlomHJ, BosGMJ, Brie tE, ReitsmaPH, Vandenbroucke JP, Rosendaal FR.
- [6]. Hyperhomocysteinemia as a risk factor for deep vein thrombosis. *N Engl J Med*. 1996;334:759-762.
- [7]. den Heijer M, Rosendaal FR, Blom HJ, Gerrits WBJ, Bos GMJ. Hyper- homocysteinemia and venous thrombosis: a meta-analysis. *Thromb Haemost*. 1998;80:874-877.
- [8]. Ray JG. Meta-analysis of hyperhomocysteinemia as a risk factor for venous thromboembolic disease. *Arch Intern Med*. 1998;158:2101-2106.
- [9]. Tiede DJ, Tefferi A, Kochhar R, Thompson GB, Hay ID. Paraneoplastic cholestasis and hypercoagulability associated with medullary thyroid carcinoma. Resolution with tumor debulking. *Cancer* 1994; 73:702-5.
- [10]. DaifA, AwadaA, al-RajehSetal. Cerebralvenousthrombosisinadults. A studyof 40 cases from Saudi Arabia. *Stroke* 1995; 26:1193-5.
- [11]. de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Case-control study of risk of cerebral sinus thrombosis in oral contraceptive users and in [correction of who are] carriers of hereditary prothrombotic conditions. The Cerebral Venous Sinus Thrombosis Study Group. *BMJ* 1998; 316:589-92.
- [12]. Saadatnia M, Tajmirriahi M. Hormonal contraceptives as a risk factor for cerebral venous and sinus thrombosis. *Acta Neurol Scand* 2007; 115:295-300.
- [13]. Allroggen H, Abbott RJ. Cerebral venous sinus thrombosis. *Postgrad Med J* 2000; 76:12-5.
- [14]. Martinelli I, Battaglioli T, Pedotti P, Cattaneo M, Mannucci PM. Hyper- homocysteinemia in cerebral vein thrombosis. *Blood*. 2003;102: 1363-1366.
- [15]. Kang S-S, Zhou J, Wong PWK, Kowalisy J, Strokosch G. Intermediate homocysteinemia: a thermolabile variant of methylenetetrahydrofolate reductase. *Am J Hum Genet*. 1988;43:414-421. 15.Frosst P, Blom HJ, Milos R, Goyette P, Sheppard CA, Matthews RG, Boers GJH, den Heijer M, Kluijtmans LAJ, van den Heuvel LP, Rozen R. A candidate genetic risk factor for vascular disease: a common mutation in methylenetetrahydrofolate reductase. *Nat Genet*. 1995;10:111-113.