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Correlation of Vitamin B12 with Homocysteine Levels in Cerebral Venous Sinus Thrombosis

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Keywords:
Vitamin B12, Homocysteine, Cerebral sinus venous thrombosis, Prothrombotic conditions

Abstract
Introduction: In geriatric individuals,Stroke is the third most frequent cause of disability. A stroke is caused by cerebral venous sinus thrombosis between 0.5 and 3.0% of the time, primarily younger people are affected and has an incidence of three–four adults per million. Previous studies have stated that Hyper-Homocystenemia is associated with venous thromboembolism and atherosclerotic arterial disease, but the relationship between vitamin B12 deficiency, Hype-Homocystenemia and Cerebral venous thrombosis remains debatable. Thus the present study was undertaken to estimate and correlate the serum level of Vitamin B 12 and homocysteine in cerebral venous sinus thrombosis (CVST) patients.
AIM & Objectives :To estimate and correlate Vitamin B12 with Homocysteine levels in cerebral venous thrombosis
Materials and methods: From January 2021 to July 2022, we conducted a hospital-based prospective observational study with a sample size of 55 patients who were admitted to BLDE (DU)'s B.M. Patil Medical College and Hospital, Vijayapura, with a clinical history and neurological examination correlating with cerebral venous thrombosis and radiological evidence. We excluded Patients who are on Drugs causing vitamin B12 deficiency, on drugs or with health conditions interfering with homocysteine metabolism and who are on vitamin B 12 supplementation. Detailed clinical history was taken and complete neurological examination was done for every subject included in the study. Fasting serum homocysteine and B12 levels were measured in all subjects. Using SPSS software, version 25, a descriptive analysis of each variable included in the study was carried out. Statistical significance was defined as P values of 0.05 or less.
Results:The proportion of vitamin B12 among various homocysteine levels varied statistically significantly with p value of <0.001. Maximum vitamin B12 deficient patients were observed in mild to moderate levels of Homocysteine. Homocysteine level and other parameters like GCS score, Prothrombin Time, Platelets counts and Hb level were not statistically correlated but Homocysteine level and Vitamin B12 level was significant negatively correlated at 10% level of significance.
Conclusion:Serum homocysteine level has significant negative correlation with vitamin B12 levels in patients with cerebral venous sinus thrombosis.

1. Introduction:

Stroke is the third most frequent cause of disability in geriatric individuals. CVT accounts for 0.5–3.0% of stroke cases, primarily younger people are affected, and has an incidence of three–four adults per million[1] . It is often associated with increased death rate[2].In recent years, the incidence of CVT has been increased due to the availability of advanced imaging techniques which helps in early detection of the disease[3]. Increased incidences have been observed in young adults, children, reproductive age group females and in countries with low economy[4]. CVT can present a diagnostic challenge owing to its varied clinical presentation (including blurred vision, headache, altered sensorium, thunderclap headache, raised intracranial pressures resulting in cranial nerve palsies with focal neuro deficit and seizures) which makes it difficult to differentiate from other neurological disorders[5]. Therefore, the diagnosis of cerebral venous thrombosis requires a greater index of suspicion. Neuroimaging is necessary for the diagnosis of cerebral venous thrombosis. The commonly reported site of occurrence includes internal cerebral vein, vein of galen, jugular vein, cortical veins, straight sinus, superior sagittal sinus and transverse sinus in ascending order[6].

Previous studies have stated that Hyper-Homocystenemia is associated with venous thromboembolism and atherosclerotic arterial disease, but the relationship between vitamin B12 deficiency,

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Hyper-Homocystenemia and CVT remains debatable. Some studies have stated that Hyper-Homocystenemia and deficiency of B12 both are major risk factors for CVT [7,8] while others have not found any relationship between vitamin B 12 and CVT [9,10]. In order to quantify and correlate the serum levels of homocysteine and vitamin B 12 in patients with cerebral venous sinus thrombosis (CVST), the current investigation was conducted.

Aim of our study is to estimate and correlate Vitamin B12 with Homocysteine levels in cerebral venous thrombosis

2. Materials and Methods:

Study design and participants:

We conducted a hospital-based prospective observational study on patients hospitalised to BLDE (DU)'s B.M. Patil Medical College and Hospital, Vijayapura, who had radiological evidence of cerebral venous thrombosis as well as a clinical history and neurological examination corresponding with it. The study was conducted period from January 2021 to July 2022.We excluded Patients who are on Drugs causing vitamin B12 deficiency, on drugs or with health conditions interfering with homocysteine metabolism and who are on vitamin B 12 supplementation. Sample size calculated with anticipated Prevalence of high levels of homocysteine in CVT patients of 70.7% , with a 95% level of confidence and 12% absolute precision was 55. Patients were selected by using simple random sampling method.

Procedure and variables assessment

Detailed clinical history was taken and complete neurological examination was done for every subject included in the study. Fasting serum homocysteine and B12 levels were measured in all subjects. Homocysteine levels were measured using Eurolyser smart 700/340 machine by

Liquid chromatography-tandem mass spectrometry method in a 1ml blood sample collected in Plasma EDTA container. Subjects were categorised into 4 groups based on their serum homocysteine levels as Normal Level (4 -15 nmol/L) , Mild Hyper-Homocystenemia(15-30 nmol/L) , Moderate Hyper-Homocystenemia(30 -100 nmol/L) and Severe Hyper-Homocystenemia(>100 nmol/L). Vitamin B12 levels were measured using Beckman Coulter Access 2 by immuno-enzymatic assay method in a 0.6ml serum sample. Subjects were categorised into 4 groups based on their serum B12 levels as Severe Deficiency(<100 pg/ml) , Mild Deficiency (100-189 pg/ml) , Normal Range (190-900 pg/ml) , High levels (>900 pg/ml).

Statistical analysis

Using SPSS software, version 25, a descriptive analysis of each variable included in the study was carried out. For analysis, numerical data were presented as a mean and standard deviation. Categorical data were shown as percentages and proportions. Data that was categorical was analysed using the Chi-square test. To analyse numerical data with a non-normal distribution, the Man-Whitney test was utilised.The Pearson correlation coefficient was discovered to ascertain the relationship between variables. Statistical significance was defined as P values of 0.05 or less.

Study protocol was reviewed and approved by institutional ethics committee.

3. Results:

Table1 shows distribution of baseline characters in sample. Out of a total 55 subjects included in the study, 29(52.7%) are males. Among total study population, 3.6% of subjects were of less than 20 years old, with maximum (52.7%) number of subjects between 21-40 years . Most of the subjects(85.5%) included in the study have no comorbidities. Among the subjects with comorbidities diabetes and hypertension are more commonly observed.18.2% of subjects have normal homocysteine levels with subjects falling under mild - moderate hyper homocystenemia with a cumulative percentage of 74.5%. 7.3% of subjects have sever hyper homocystenemia. Coming to the distribution of levels of vitamin B12 among study population, 45.5% of subjects have severe B12 deficiency with 25.5% with mild deficiency.30% of subjects were reported to have normal vitamin B12 levels. Among study population 90.9% have normal platelet values with 72.7% with GCS of more than 13.Figure 1 shows site of thrombosis in different subjects with maximum frequency in left occipital and temporal regions. Figure 2 shows distribution of sinus involvement among study population with max frequency in superior sagittal sinus. Figure 3 shows distribution of symptoms among study population with maximum number of subjects experiencing headache

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Table 1: Description of the sample: baseline characteristics

Variables-Baseline characters	N=50
Sex, male, n(%)	29(52.7%)
Age distribution(groups) <20years,n(%) 21-40years,n(%) 41-60years,n(%) 61-80years,n(%)	 2(3.6%) 29(52.7%) 12(21.8%) 12(21.8%)
Comorbidities HTN, n(%) DM, n(%) Epilepsy, n(%) No comorbids, n(%)	 6(10.9%) 4(7.2%) 3(5.5%) 47(85.5%)
Homocysteine levels (groups) Normal Level (4 -15 nmol/L) Mild Hyper-Homocystenemia(15 – 30 nmol/L) Moderate Hyper-Homocystenemia(30 -100 nmol/L Severe Hyper-Homocystenemia(>100 nmol/L)	 10(18.2%) 22(40%) 19(34.5%) 4(7.3%)
Vitamin B12 levels(groups) Severe Deficiency(<100 pg/ml) Mild Deficiency (100-189 pg/ml) Normal Range (190-900 pg/ml)	 25(45.5%) 14(25.5%) 16(30%)
Haemoglobin levels <10 gm/dl	 9(16.4%)

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10-15 gm/dl >15 gm/dl	38(69.1%) 8(14.5%)
Platelet count <1.5lakhs/microlitre >1.5lakhs/microlitre	 5(9.1%) 50(90.9%)
Glasgow coma 9-12 13-15	 15(27.3%) 40(72.7%)

Figure 1: Distribution of thrombosis among study population

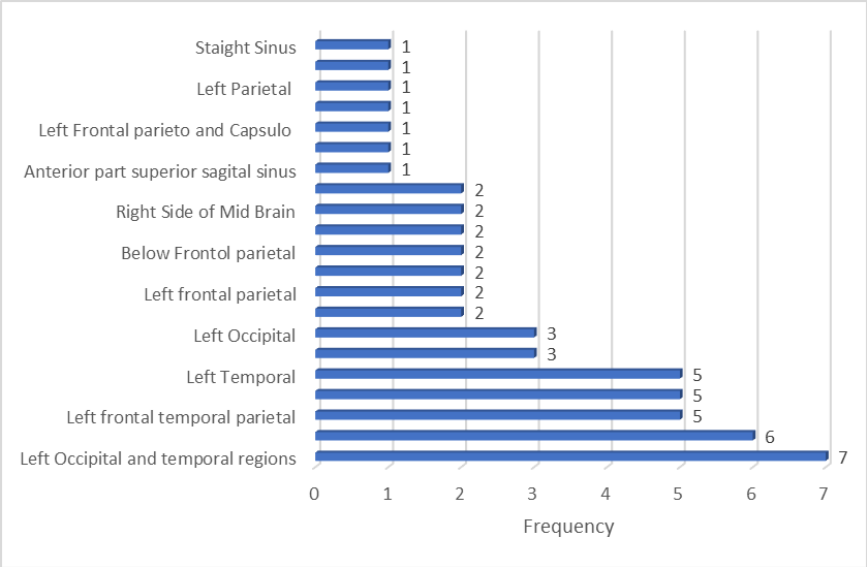

Figure 2 : Distribution of sinus involvement among study population

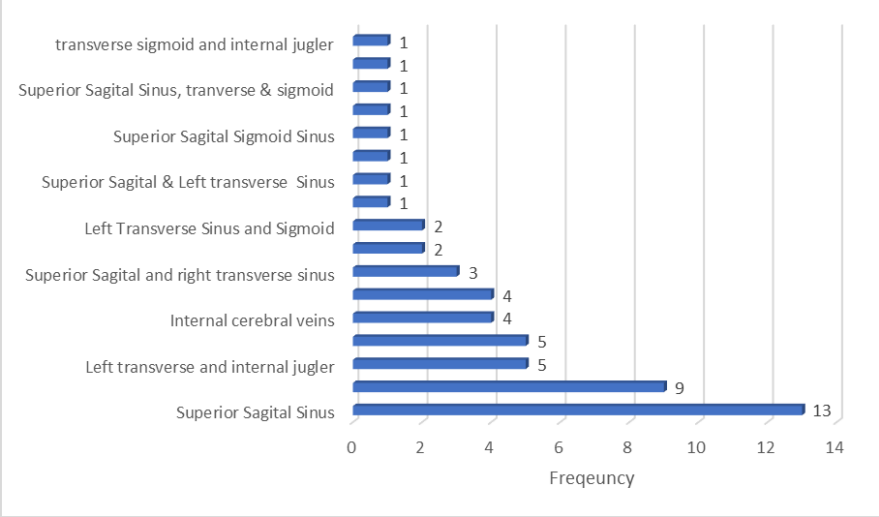

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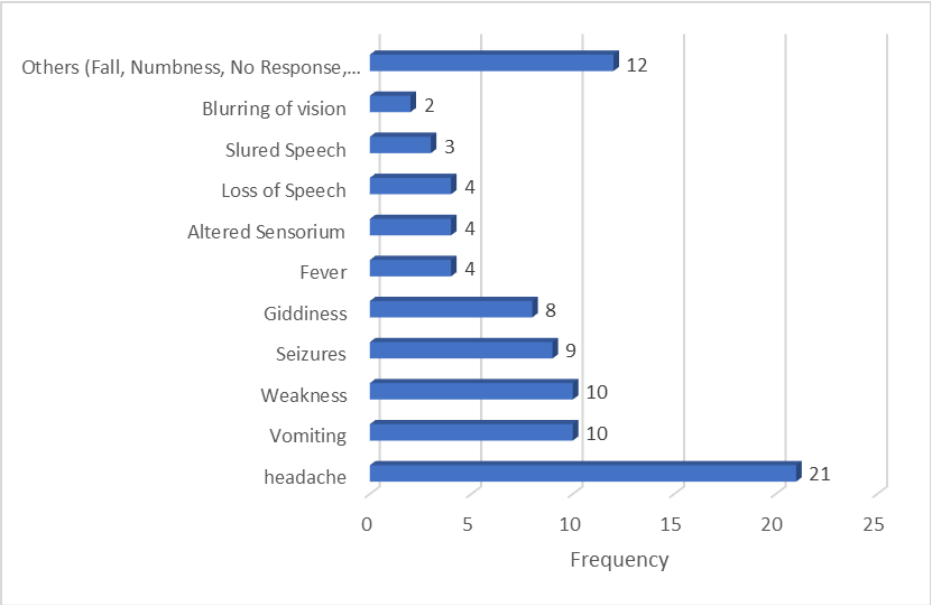
Figure 3: Distribution of symptoms among study population



Distribution of homocysteine levels and vitamin B12 levels among both the genders and different age groups has been analysed with chi square test and found that difference was not significant. Different lab parameters including HB, MCV, MCH, ESR, Platelet count, prothrombin time and GCS has been analysed in groups with normal and raised homocysteine levels and found to have no significant difference. Table 2: Vitamin B12 levels in different homocysteine level groups.We have observed the proportion of vitamin B12 among various homocysteine levels varied statistically significantly with p value of <0.001. Maximum vitamin B12 deficient patients were observed in mild to moderate levels of Homocysteine. Table 3 shows Correlation between Homocysteine level with vitamin B12 and other parameters. Homocysteine level and other parameters like GCS score, Prothrombin Time, Platelets counts and Hb level were not statistically correlated but Homocysteine level and Vitamin B12 level was significant negatively correlated at 10% level of significance.

Homocysteine Intervals	Vitamin B12			Total	Chi-square	P-value
	< 100 pg/ml	100-189 pg/ml	190-900 pg/ml			
4- 15 nmol/L.	1(1.80%)	6(10.90%)	3(5.50%)	10(18.20%)	18.8**	0.001
15 - 30 nmol/L.	7(12.70%)	4(7.30%)	11(20.0%)	22(40.0%)		
30 - 100 nmol/L.	13(23.60%)	4(7.30%)	2(3.60%)	19(34.50%)		
> 100 nmol/L.	4(7.30%)	0(0%)	0(0%)	4(7.30%)		
Total	25(45.50%)	14(25.50%)	16(29.10%)	55(100%)		

Table 2: Vitamin B12 levels in different homocysteine level groups

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Homocysteine levels	vitaminB12	GCS Score	Prothrombin time	Platelets Count	Hb Level
Pearson Correlation	-0.26	0.14	-0.038	-0.06	0.027
Significance	0.05	0.309	0.783	0.662	0.846
N	55	55	55	55	55

Table 3: Correlation between Homocysteine level with vitamin B12 and other parameters.

4. Discussion:

Due to the ambiguous nature of its clinical and radiological presentation, CVST is a neurological disorder that is very uncommon, potentially lethal, and frequently goes undiagnosed. Numerous conditions, such as sinusitis, trauma, surgery, hypercoagulable states (like antiphospholipid syndrome, protein C and protein S deficiency, and anti-thrombin deficiency), vasculitis, pregnancy, puberty, use of OCPs, nephrotic syndrome, malignancy, etc., can happen alone or in combination to predispose to cerebral venous thrombosis. The majority of CVT risk factors that are implicated are prothrombotic diseases.

Homocysteine is an alpha amino acid derived from methionine. Homocysteine is normally transformed to cysteine through the transsulfuration pathway which is then eliminated by urinary system. In this route, pyridoxine is needed as a cofactor. Remethylation pathway, uses methylene tetrahydrofolate reductase (from the metabolism of folate), for converting homocysteine back to methionine in which vitamin B12 is a cofactor . These two important pathways control the metabolism of homocysteine ,hence any disorder in this route Hyper-Homocystenemia results [15]. As Folate, vitamin B12, and vitamin B6 participate in these pathways, deficiency of these vitamins leads to hyper-homocystenemia. Patients with chronic conditions including diabetes and cancer as well as advanced age, males, postmenopausal status females, extensive smoking history, are shown to have higher amounts. They are also seen after the administration of specific medications like oral contraceptives, anti-epileptic Drugs, and methotrexate.

Prior to the development of antibiotics, CVT was thought to be caused by infections of the face and otomastoid regions. Today, however, it is usually connected to oral contraceptives, hereditary and acquired thrombophilia, puerperium, neoplasms, dehydration, and pregnancy [6,11-13]. The hypercoagulability brought on by using oral contraceptives, particularly in Western nations, increases the risk of cerebral venous thrombosis [5,14,15]. Oral contraceptive use and the prothrombin gene mutation (G20210A) both increased the risk of cerebral venous thrombosis by odds ratios of 10 and 22, respectively. The chances ratio increases considerably to 150 when both the prothrombin mutation and oral contraceptive usage are present [5]. In many studies they observed the correlation of cerebral venous thrombosis and homocysteine also they found that the association of CVT and Hyper-Homocystenemia present. Additionally, they found that total homocysteine continues to be an important risk factor for CVST in subjects with confirmed thrombosis [9,10]. These studies also had the restriction of estimating homocysteine along with vitamin B12 in thrombosis. Thus, we have undertaken this study with aim to estimate the levels of vitamin b12 and homocysteine in subjects with CVT and estimate the correlation of vitamin b12 and homocysteine in subjects with CVT.

Study conducted by Sanskriti Kamran et al [6] observed that most common age group of presentation with CVT are 21-40 years :71.05% with a slight male (60.53%) prevalence similar to our study. Another study by Sohan B et al[10] also observed that majority were from age group of 31- 40 years with male preponderance (66.13 %) . Makoto Takemaru et al. [11]conducted a study to identify the incidence, clinical features, and risk factors of Japanese patients with cerebral venous thrombosis. They found that the mean age of patients was 37 years old and 74.5% of the patients were female, which is contrary to our study's findings in regards to gender. According to a study by M.A. Al Baklawy et al [15], the superior sagittal sinus (SSS), the lateral sinus (LS), both sinuses, the straight sinus, and the internal jugular vein were all occluded in 12 cases (75.0%), 11 cases (68.8%), and 7 cases (43.8%), respectively. Another study by Sanskriti Kamran et al [6] most affected are left transverse & sigmoid sinuses (55.26%) followed by right transverse

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sinus & sigmoid sinuses (35.53%). Study by Makoto Takemaru et al [11] observed superior sagittal sinus in 12 instances (75.0%), lateral sinus in 11 subjects (68.8%), both sinuses in 7 subjects (43.8%), straight sinus in 4 subjects (25.0%), and internal jugular vein in 1 subject (6.3%), were the obstructed sinus or cerebral vein. In our study We have observed that, majorly Superior Sagittal Sinus, Left Sigmoid & transverse Sinus, left transverse and internal jugular, Diffuse Venous Sinus etc involved in cerebral venous thrombosis patients. Major symptoms among maximum patients were headache followed by vomiting, weakness, seizures, and giddiness with 62.5% of people experiencing headache. Similar to our study another study by M.A.Al Baklawy et al[15] observed that, the frequency of clinical symptoms varied; it ranged from 81% to 98% for headaches, 27-76% for seizures, 10-64% for unconsciousness, and 27% to 76% for localised neurological impairments. Present study noticed that among all the patients 74.5% of the patient's homocysteine was in the range of mild to moderate Hyper-Homocystenemia. Levels of Hyper-Homocystenemia was maximum among male(89.6%) compared to female(73.07%), but this difference in the proportion between male and female was statistically not significant (P-value =0.136). In the age group of 41- 60 years percentage of the patients with mild to moderate homocystenemia was 91.60% whereas in the age group of 21 – 40 years it was 82.74% .Study by M.A.Al Baklawy et al [15]56.3% of the patients with cerebral venous sinus thrombosis had higher serum homocysteine levels, according to their study. Another study by Sanskriti Kamran et al [6]observed that, of 76 patients of cerebral venous thrombosis, 52 patients had hyper-homocystenemia, out of which 16 patients had moderate hyper-homocystenemia, 36 patients had intermediate Hyper-Homocystenemia . One more similar study to our's by Manasi Harale et al [8] on 50 patients,35 patients had high serum homocysteine levels. The available research states that Hyper-Homocystenemia is a significant contributor to hyper coagulopathy and four times more likely to induce CVT. Homocysteine levels should therefore be considered in the early prothrombotic workup for idiopathic venous thrombosis. Studies by Carlos Cantu et al , Taheraghdam, et al. , Sohan B et al, Patel J. D. et al. showed raised levels of homocysteine is associated with CVT. According to research by E. Oger et al, venous thromboembolism is an independent risk factor for moderately increased fasting homocysteine levels. Adjusting for potential confounding factors like folates or vitamin B12 had no discernible impact on the outcome. Our study population had vitamin B12 deficiency among 71% of the patients, with 45.5% of the patients having severe deficiency and 25.5% with moderate deficiency; No difference was observed in the Vitamin B12 levels between male and female as well as in different age groups. M.A.Al Baklawy et al [15]showed deficiency of vitamins like B12 cause hyperhomocystenemia and also added that Hyper-Homocystenemia in cerebral venous thrombosis can be treated with vitamin supplements, dietary adjustments, and lifestyle modifications.

Patients with cerebral venous thrombosis in a related study by Manasi Harale et al[8] did not show any correlation between their vitamin B12 levels. The study found that whereas homocystine levels are more likely to be high when vitamin B12 levels are low, hyperhomocystenemia may not always be associated with low vitamin B12 levels. Low levels of folate and vitamin B12 were found to be related with a higher risk of CVT in the population, Carlos Cantu et al. [16] concluded, suggesting that the condition's relatively high incidence may be due to its low socioeconomic and nutritional status. Kalita et al [17] observed that, the three vitamins B12, pyridoxine, and folic acid are necessary for homocysteine metabolism. Hyper-Homocystenemia is caused by a deficit in these vitamins through trans-sulfuration or remethylation pathways .Cantu et al. [16] discovered that raised levels of homocysteine and low vitamin B12 levels had separate associations with the incidence of CVT. In this study we have found negative correlation between homocysteine and vitamin B12. Similar to our study Patel J. D. et al Deepak Arthur observed there was negative correlation coefficient between vitamin B12 and homocysteine (r=-0.148, p-value =0.02) also they found there was lower level of vitamin B12 among cases compared to control group. One more study by Deepak Arthur also found Homocysteine levels have a negative relation with vitamin B12 levels (Pearson correlation coefficient: 0.3874; P = 0.0005). These findings lend credence to the study, and we discovered a highly significant correlation between homocysteine levels and vitamin B12 levels.

5. Conclusion:

Our findings lend support to the hypothesis that hyperhomocystenemia is linked to a higher risk of CVT

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and that a high risk of cerebral venous thrombosis was strongly correlated with low vitamin B12 levels, based on overall observation and discussion with other studies. In addition, levels of homocysteine and vitamin B12 are negatively correlated. Since supplemental medication can be used to reduce these acquired risks and prevent CVT from recurring, long-term studies with high sample sizes are required to determine the mechanism and effect of Hyper-Homocystenemia, low vitamin B12, on the risk of CVT.

Bibliography:

[1] Idiculla PS, Gurala D, Palanisamy M, Vijayakumar R, Dhandapani S, Nagarajan E. Cerebral Venous Thrombosis: A Comprehensive Review. Eur Neurol. 2020;83(4):369-379. doi: 10.1159/000509802. Epub 2020 Sep 2. PMID: 32877892.

[2] Kataria N, Yadav P, Kumar R, et al. (May 11, 2021) Effect of Vitamin B6, B9, and B12 Supplementation on Homocysteine Level and Cardiovascular Outcomes in Stroke Patients: A Meta-Analysis of Randomized Controlled Trials. Cureus 13(5): e14958. DOI 10.7759/cureus.14958

[3] Bousser MG, Ferro JM. Cerebral venous thrombosis: An update. Lancet Neurol. 2007;6:162–70.

[4] Ferro JM, Canhão P. Cerebral venous sinus thrombosis: update on diagnosis and management. Curr Cardiol Rep. 2014; 16(9): 523.

[5] Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F. 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.

[6] Stam J. Thrombosis of the cerebral veins and sinuses. N Engl J Med. 2005 Apr 28;352(17):1791-8. doi: 10.1056/NEJMra042354. PMID: 15858188.

[7] Taheraghdam AA, Dalirakbari N, Khalili M, Soltani M, Ahari SS. Hyper-homocystenemia, low vitamin B12, and low folic acid: Are risk factors of cerebral vascular thrombosis in northwest Iran? J Res Med Sci 2016;21:16.

[8] Harale M, Alurkar A, Basavaraj A, Kadam DB, Chandanwale A. Co-relation of Cerebral Venous Sinus Thrombosis with Vitamin B12 and Homocysteine Levels in a Tertiary Care Centre. J Assoc Physicians India. 2019 Jan;67(1):34-37. PMID: 30935170

[9] Kamran S, Sharma S, Banerjee S, Thakur SD. Correlation Between Cerebral Venous Sinus Thrombosis And Serum Homocysteine Levels In A Tertiary Care Hospital, India A Prospective Observational Study. International Journal of Advanced Research. 2021;9(1):251-74. 10.21474/IJAR01/12302.

[10] Sohan B, Hamsa Manasa K. Co-relation of cerebral venous sinus thrombosis with vitamin B12 and homocysteine levels in a tertiary care centre. MedPulse International Journal of Medicine. March 2022; 21(3): 65-69

[11] Takemaru M, Kuriyama M, Himeno T, Shiga Y, Kanaya Y, et al. (2017) Cerebral Venous Sinus Thrombosis: Incidence and Hyper-Homocystenemiaas a Risk Factor in Japanese Patients. J Neurol Neurosci. Vol. 8 No. 5:219

[12] J.M.Coutinho, Cerebral venous thrombosis. J Thromb Haemost ,Vol.13, PP. 238– 244,2015.

[13] Coutinho JM, Stam J, Canhao P (2015) Cerebral venous thrombosis Is the absence of headache. Stroke 46: 245-247.

[14] Shindo A, Wada H, Ishikawa H (2014) Clinical features and underlying causes of cerebral venous thrombosis in Japanese patients. Int JHematol 99: 437-440.

[15] Baklawy, M., Khodair, R, Faheem, M., Abd Elrassoul, I. Serum Homocysteine level in patients with cerebral venous Sinus Thrombosi(CVST):Relation to initial Thrombosis Severity and Outcome, Benha Journal of Applied Science, 2020; 5 Issue1 Part (1)

[16] Carlos Cantu, Elisa Alonso, Aurelio Jara, Leticia Martinez, Camilo Rios, Maria de los Angeles Fernandez ImaGracia, Fernando Barinagarrementeria. Hyper-homocystenemia, Low Folate and Vitamin B12 concentrations and Methylene TetrahyDRofolateReductase in Cerebral Venous Thrombosis. 2003; accepted April 21,2004.

[17] Kalita J, Singh VK, Misra UK. A study of Hyper-Homocystenemiain cerebral venous sinus thrombosis. Indian J Med Res. 2020 Dec;152(6):584-594. doi: 10.4103/ijmr.IJMR_2125_18. PMID: 34145098; PMCID: PMC8224164