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General Medicine

A STUDY OF SERUM HOMOCYSTEINE LEVELS IN PATIENTS WITH CEREBRAL SINUS VENOUS THROMBOSIS

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ABSTRACT

Background: Cerebral sinus venous thrombosis(CSVT) is the distinctive cause of cerebrovascular disease in young adults. Clinical manifestations of CSVT are variable and includes headache, blurred vision, altered sensorium, with raised ICP leading to cranial nerve palsies with focal neurological deficits and seizures. The important prothombotic states which predispose to CSVT include hyperhomocysteinemias.

Objective: To study Serum Homocysteine levels in patients with cerebral sinus venous thrombosis

Materials and Methods: 40 patients having Cerebral Venous Thrombosis were diagnosed by brain imaging. Every patient was subjected to a detailed clinical history and neurological examination. In each patient fasting serum homocysteine levels and serum B12 levels were analyzed. The serum homocysteine levels were done by ELISA. On the basis of serum homocysteine levels, the patients were divided into 4 categories: Normal Level, Moderate Hyperhomocysteinemia, intermediate Hyperhomocysteinemia and Severe Hyperhomocysteinemia.

Results: Of the 40 patients, 25(62.5%) are males and 15(37.5%) are females , 27(67.5%) patients were found to have elevated levels of homocysteine out of which 9(22.5%) patients had moderate hyperhomocysteinemia, 18(45%) had intermediate homocysteinemia and 13(32.5%) had normal levels of serum homocysteinemia

Conclusion: The study had shown that homocysteine levels were significantly higher in CSVT patients and serum hyperhomocysteinemia is one of the risk factor in the etiology of Cerebral Venous Sinus Thrombosis patients.

KEYWORDS :

INTRODUCTION

Thrombosis of the dural sinuses / cerebral veins is an uncommon form of stroke, usually affecting young individuals[1]. Magnetic resonance imaging and magnetic resonance venogram are the best diagnostic methods for diagnosis of CVST and heparin is the first-line of treatment.

It is one of the commonest causes of stroke in India. CVST usually occurs in the setting of pregnancy and puerperium. CVST in the nonpuerperal setting is less common. The pathological hallmark of CVST is hemorrhagic infarction. CVST can present in protean ways with a wide spectrum of clinical manifestations. These include headache, altered sensorium, seizures, focal neurological deficits, papilloedema and cranial nerve palsies. Headache is the most frequent and often the earliest manifestation[2]

The diagnosis of cerebral venous sinus thrombosis requires high index of suspicion. CT brain may show direct or indirect signs of cerebral venous thrombosis. It may be normal in 10% of patients. In such cases advanced neurological diagnostic like Magnetic Resonance Imaging with venography is necessary to confirm cerebral sinus venous thrombosis. It has been found that early diagnosis of cerebral sinus venous thrombosis is essential because early treatment may prevent morbidity and may even be life saving.

The important prothrombotic states which predispose to the development of CVT include Factor V Leiden mutation, antiphospholipid antibody syndrome, Protein C deficiency, Protein S deficiency, antithrombin III deficiency, fibrinogen deficiency, polycythemia rubra vera, paroxysmal nocturnal hemoglobinuria, sickle cell disease, haemolytic anaemia, thrombocythemias and hyperhomocysteinimias. Recently, Factor VIII elevation has also been identified as a thrombophilic factor which can cause CVST. Among the thrombophilic states, Factor V Leiden mutation has been identified as the commonest hereditary prothrombotic state while APLA syndrome is the commonest acquired prothrombotic state.

Persons homozygous for homocysteinuria are at high risk for premature arteriosclerotic vascular disease and venous thrombosis, as homocysteine is toxic to vascular endothelium, can potentiate the oxidation of low density lipoprotein cholesterol and promote thrombosis[3]

Homocysteine (Hcy) is a sulfhydryl amino acid compound that is generated from protein breakdown and the essential amino acid methionine as it is metabolized to cysteine. Hcy can be metabolized by two major pathways When methionine is in excess, Hcy is directed to the transulphuration pathway, where it is irreversibly sulfoconjugated to cysteine by cystathionine B-synthase with vitamin B6 as a cofactor. Hcy is also remethylated in a methionine-conserving pathway. This process requires methionine synthase, vitamin B12 as a cofactor, and methyltetrahydrofolate as a cosubstrate. The methionine-conserving pathway requires folic acid and methyltetrahydrofolate reductase (MTHFR). There is a strong inverse correlation of plasma Hcy with plasma folate concentration. In contrast to folate, serum vitamin B12 or vitamin B6 levels show only a weak correlation with plasma Hcy. Deficiencies in any of these above enzymes, folic acid, or the cofactors may lead to some degree of hyperhomocysteinemia[4]. Hyperhomocysteinemia is a risk factor for deep vein thrombosis and stroke but has not been clearly associated with an increased risk of CVT

PATIENTS AND METHODS

Patients of Cerebral Venous thrombosis who were admitted in NRI institute of medical sciences and anil neerukonda hospital, Visakhapatnam, were included in this study. We have taken sample size of 40 patients of Cerebral Venous Thrombosis from August 2019 to May 2021 for fasting homocysteine and serum B12 level. Every patient was subjected to a detailed clinical history and neurological examination.MRI brain and venogram were done. In each patient fasting serum homocysteine levels and serum B12 levels were done. The serum homocysteine levels and VIT B12 were analyzed by ELISA.

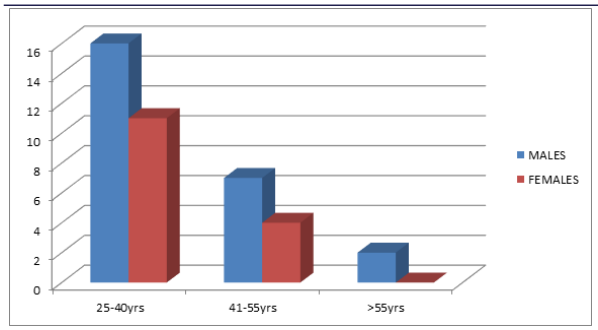
On the basis of serum homocysteine levels, the patients were divided into 4 categories: Normal Level, Mild Hyperhomocysteinrmia, Moderate Hyperhomocysteinemia and Severe Hyperhomoc ysteinemia.

1. Normal Levels : 4 -15 nmol/L.
2. Mild Hyperhomocysteinemia: 15 – 30 nmol/L
3. Moderate Hyperhomocysteinemia : 30 – 100 nmol/L
4. Severe Hyperhomocysteinemia : >100 nmol/L

RESULTS :

Table 1 : Age And Gender Distribution

Age	Males	Females	Total
25-40 yrs	16	11	27
41-55yrs	7	4	11
>55yrs	2	0	2
Total	25	15	40



Out of 40 patients
27(67.5%) were in age group 25-40 yrs, 11(27.5%) patients were in age group 41-55 yrs and 2(5%) are above 55 yrs.
25(62.5%) are males and 15(37.5%) are females.

Table 2 : Serum Homocysteine Levels

Homocysteine levels	N	%
Normal(<15)	13	32.5%
Moderate (15-30)	9	22.5%
Intermediate(30-100)	18	45%
Severe(>100)	0	0
Total	40	100%

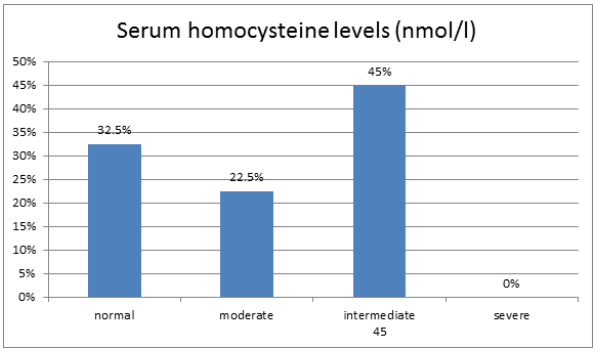


Table 3 Comorbidities

	N	%
HTN	**7**	17.5%
T2DM	1	2.5%
HTN+T2DM	9	22.5%
Nil	23	57.5%

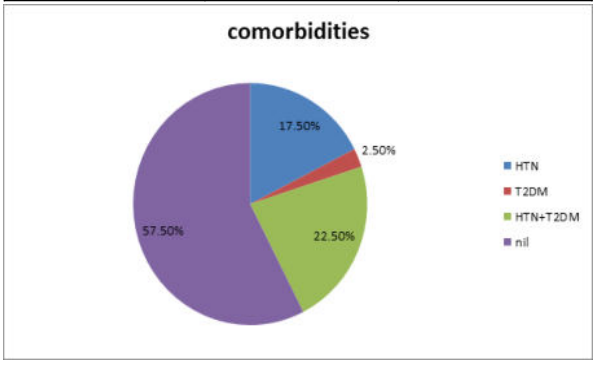


Table 4 : Correlation of S.homocysteine levels with age

Age	Normal	Moderate	Intermediate	Severe	Total
25-40yrs	9	5	13	0	27
41-55yrs	2	4	5	0	11
>55yrs	2	0	0	0	2
	13	9	18	0	40

Table 5 : Correlation of S.homocysteine levels with gender

Gender	Normal	Moderate	Intermediate	Severe	Total
Males	7	6	12	0	25
Females	6	3	6	0	15
	13	9	18	0	40

DISCUSSION:

This observational comparative study was done at NRI institute of medical sciences Visakhapatnam , from august 2019 to may 2021and involved 40 patients of Cerebral Venous Sinus Thrombosis. With the help of clinical evaluation and detailed investigations we had determined hyperhomocyseinemia is the risk factor for Cerebral Venous Sinus Thrombosis. 67.5% patients were found to have high homocysteine level either moderate or intermediate. Data obtained from these patients were analyzed and the results were compared with prior studies of similar objectives. We also found in our study that most common age group of presentation with CVST are: 25-40 yrs with incidence of 67.5% with a slight male (62.5%) prevalence in comparison to female (37.5%). In 57.5% of patients no associated comorbidity was found in the study population. No statistical significance could be derived between serum homocysteine and age or gender of the patients.

Correlation between Serum Homocysteine levels and Cerebral Venous Sinus Thrombosis: In the present study of 40 patients of CVST, 27 patients had hyperhomocysteinemia, out of which 9 patients had moderate hyperhomocysteinemia, 18 patients had intermediate hyperhomocysteinemia and 13 patients had normal levels of serum homocysteine. The mean of serum homocysteine levels was 25.91 ranging from 10.57 to 55.69.

In a similar study conducted by **ManasiHarale et al** on 50 patients, 35 patients were found to have elevated serum homocysteine levels. According to the published literature, hyperhomocysteinemia is an important cause of hypercoagulopathy and increases risk of CVST by 4 folds. Therefore, it would be prudent to include homocysteine levels in initial prothrombotic workup for unprovoked venous thrombosis[5].

In a similar study conducted by **Carlos Cantu et al** on 45 patients of CVST, concluded that high plasma concentrations of homocysteine were associated with an increased risk of Cerebral Venous Thrombosis[6].

In a similar study conducted by **VenkataPinnelliBharatkumar** et al in 185 patients with aseptic CVT concluded that hyperhomo cysteinemia is a risk marker for Indian patients with aseptic CVT[7].

A study by **Ida Martenelli** et al in 121 patients with first episode of CVT was conducted and concluded that hyperhomocysteinemia is associated with a 4- fold increased risk of cerebral venous thrombosis and its correlation with vitamins to reduce the risk of the disease was not clearly demonstrated[8]. This study was conducted in Italy which has different demography as compared to our study population.

CONCLUSION:

In conclusion hyperhomocysteinemia could be a risk factor accounting for Cerebral Venous Sinus Thrombosis. The results of this study have shown that homocysteine levels were significant in CVST patients and serum hyperhomocysteinemia is a risk factor in the etiology of Cerebral Venous Sinus Thrombosis patients.

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