“CORRELATION OF CEREBRAL VENOUS SINUS THROMBOSIS WITH VITAMINB12 AND HOMOCYSTEINE LEVELS”

BY

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LIST OF ABBREVATIONS

CVT	-	Cerebral venous thrombosis
Hcy	-	Homocysteine
CVD	-	cardiovascular diseases
ISCVT	-	International Study on Cerebral Vein and Dural Sinus Thrombosis
MTHFR	-	Methyl tetrahydrofolate reductase
GCS	-	Glasgow Coma Scale
SSS	-	Superior Sagittal Sinus
LS	-	Lateral Sinus
CAD	-	coronary artery disease
HTN	-	Hypertension
DM	-	Diabetes Mellitus

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ABSTRACT

Introduction: Compared to most other types of strokes, cerebral venous sinus thrombosis (CVT) is less frequent. It accounts for 0.5–3% of all stroke cases, primarily affecting younger people, and has an adult incidence of 3–4 per million. Through its effects on platelets, thrombin, and fibrin, high levels of homocysteine lead to oxidative damage to vascular endothelium, the growth of vascular smooth muscle, and the development of a prothrombotic milieu.

Aim & Objectives: We have undertaken this study to estimate and correlate vitamin b12 and homocysteine levels in cerebral venous sinus thrombosis

Materials and Method: This Prospective observational hospital-based study conducted on 55 patients of cerebral venous thrombosis admitted after following inclusion criteria and getting consent form patients in our tertiary care centre during January 2021 to July 2022, BLDE B.M. Patil Medical College Hospital and Research Centre, Vijayapura.

Results: In the study we have included total 55 sample among which male were predominant over female in most age group 20-40 years. Majority of the patients had severe deficiency of vitamin B12 and it is negatively correlated with homocysteine at 10% level of significance. There was significant difference observed in the proportion of vitamin B12 among Homocysteine levels. Maximum vitamin B12 deficient patients were observed in mild to moderate levels of Homocysteine. (p-value<0.001)

Conclusion: Overall, based on our observations and findings, we can draw the conclusion that Hyper-Homocystenemia is linked to a higher risk of Cerebral Venous Thrombosis (CVT). Furthermore, a high risk for cerebral venous thrombosis was substantially associated with low vitamin B12 levels.

INTRODUCTION

Stroke is defined as “Rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting 24 hours or longer, or leading to death, with no apparent cause other than vascular origin”. It is the third most common cause of disability in geriatric individuals.[1] Cerebral venous sinus thrombosis is often associated with increased death rate.[2] It accounts for 0.5–3.0% of stroke cases, primarily younger people are affected, and has an incidence of 3–4 adults per million.[3] In recent years, the incidence of Cerebral venous thrombosis has been increased due to the availability of advanced imaging techniques which helps in early detection of the disease. Increased incidences have been observed in young adults, children, reproductive age group females and in countries with low economy.[4]

Cerebral venous thrombosis can be divided in to acute (lasting less than 48 hours), subacute (lasting between 48 hours and 30 days), and chronic (lasting longer than one month). [5] Nearly half of all occurrences of cerebral venous thrombosis are of the subacute type, which is more prevalent than the chronic variety. [6]

Clinical presentations of Cerebral venous thrombosis includes blurred vision, headache, altered sensorium, thunderclap headache, raised intracranial pressures resulting in cranial nerve palsies with focal neuro deficit and seizures.[7] 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] Cerebral venous thrombosis can present a diagnostic challenge owing to its varied clinical presentation which makes it difficult to differentiate from other neurological disorders.

Therefore, a higher index of suspicion is required for the diagnosis of cerebral venous thrombosis. The diagnosis of cerebral venous thrombosis depends on neuroimaging. [2,8] Cobalamin, also known as vitamin B12, aids in the metabolism of fatty acids and amino acids and functions as a

cofactor in the production of DNA. [9] By playing a significant role in the growth of red blood cells (RBC) and the production of myelin in the bone marrow, it contributes to the healthy operation of the neurological system. [10-12] The brain and neurological system's cells may become permanently damaged if vitamin B12 deficiency persists. [11,13] Even mild deficiency of vitamin B12 may result in lethargy, fatigue, difficulty in walking and balancing, poor memory, depression, breathlessness, pale skin, and headaches. [8,14] Around 6% of people globally are thought to be B12 deficient, with Europe accounting for 1.6–10% of that number. Older people (those over 60) have a higher prevalence, which varies between 10% and 19% globally. Additionally, females typically have a higher prevalence than males. [15]

When methionine is converted to cysteine, homocysteine, an amino acid containing sulphur, is synthesized. Hyper-Homocystenemia is the medical term for elevated amounts of homocysteine in the blood (HHcy). One of the important risk factors for cerebral, peripheral, and coronary atherosclerosis has been identified as hyper-homocystenemia. [16-19] Hyper-Homocystenemia is found in around 5% of the general population and is linked with an increased risk of many conditions such as autoimmune disorders, vascular and neurodegenerative diseases, birth defects, renal diseases, diabetes, neuropsychiatric disorders, osteoporosis, and cancer.[20]

Homocysteine levels can be raised due to a defect in the metabolism of methionine, which may be either due to mutation in the genes coding for the enzymes required for Homocysteine metabolism, or due to deficiencies of several vitamin cofactors. [21-23] pregnancy, and lactation, disease status and altered cellular export mechanisms are some of the known causes of variations in Homocysteine levels. [24-26]

Besides alterations in genetics, deficiency of vitamins and certain other factors including several medications, more intake of Methionine, Higher levels of homocysteine results in oxidative damage to the vascular endothelium and proliferation of vascular smooth muscle which creates a prothrombotic condition by its action on thrombin, platelets and fibrin.[27] Increased oxidation of

low-density lipoprotein, activation of factor V, inhibition of plasminogen activator binding and protein C activation and direct damage to the vascular endothelium are some of the probable means through which homocysteine may cause thrombosis.[28]

Previous studies have suggested a positive relationship between Hyper-Homocystenemia and Cerebral venous thrombosis, but still its pathophysiology is not well understood. studies have stated that Hyper-Homocystenemia is associated with venous thromboembolism and atherosclerotic arterial disease, but the relationship between vitamin B12 deficiency, Hyper-Homocystenemia and Cerebral venous thrombosis remains debatable. Some studies have stated that Hyper-Homocystenemia and deficiency of B12 both are major risk factors for Cerebral venous thrombosis, [29,30] while others have not found any relationship between vitamin B 12 and Cerebral venous thrombosis. [8,31] 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 AND OBJECTIVES

AIM: Estimation and correlation of Vitamin B12 and Homocysteine with cerebral venous thrombosis

OBJECTIVES:

- To estimate the levels of Vitamin b12 and Homocysteine in subjects with cerebral venous thrombosis
- To estimate the correlation of Vitamin b12 and Homocysteine in subjects with cerebral venous thrombosis

REVIEW OF LITERATURE

Cerebral Venous Thrombosis (CVT) refers to the presence of thrombus in the dural venous sinuses.[8] The approximated male to female ratio of Cerebral venous thrombosis is 1:3 and it accounts for about 0.5–1% of all stroke occurrences. [3,32] It is the commonest cause of stroke in young adults, which is reversible and treatable and thus can be avoided.[31] Stroke is one of the leading causes of physical impairment in the old age people. A stroke is defined as the sudden death of brain cells due to a lack of oxygen, a rupture in or blockage of an artery feeding the brain or eye. [1] Approximately 70% of the stroke cases were observed in the middle and low economy countries worldwide.[33] It is a predominant reason for long-term disability, responsible for decreased mobility in approximately 50% of the stroke survivors in elderly (>65 years) population. In the year 2018, stroke was held responsible for one in every six deaths due to cardiovascular diseases (CVD).[34]

According to data published by the American Heart Association, cerebrovascular illness was responsible for around 6.2 million fatalities worldwide, of which 2.7 million were attributable to ischemic stroke, 3 million to intracerebral haemorrhage, and 0.4 million to subarachnoid haemorrhage. Worldwide, certain countries of Africa, Eastern Europe and Central Asia have been reported to have the highest death rates due to stroke.[34]

The mortality rate by cerebrovascular accident in 2016 was estimated to be 1 in every 180 seconds and Cerebral venous thrombosis often presents clinically with a variety of signs and symptoms based on the patient's age, site and extent of thrombosis and the etiological factors underneath.[7] The most frequently encountered clinical features includes reduced visual acuity, headache, and papilledema as a result of raised intracranial pressure, focal neurological deficits, diffuse encephalopathy and seizures. Thunderclap headache, subarachnoid haemorrhage, tinnitus,

recurrent transient ischemic attacks, multiple cranial nerve palsies and isolated headache are some of the uncommon features of Cerebral venous thrombosis.[2,3] According to the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT), the most commonly involved site by Cerebral venous thrombosis is transverse sinus (86%) followed by superior sagittal sinus (62%), straight sinus (18%), cortical veins (17%), jugular veins (12%), vein of Galen, and internal cerebral vein (11%), in that order.[6]

Thrombosis involving the cerebral cortical veins and the cranial venous sinuses can result in a distinctive cerebrovascular disorder, which in contrast to the arterial stroke, frequently affects young adults and children. This type of cerebrovascular disorder may occur either de novo as the initial manifestation or can co-exist with another clinical problem. In both the cases, it is always variable and multifactorial in each patient. Every component of the Virchow's triad, namely, endothelial damage, stasis and hypercoagulability of blood may bear some of the contributing factors that results in full blown clinical presentation of Cerebral venous thrombosis. [35]

The conditions with higher tendency for thrombosis such as hyper-homocystenemia, dehydration, unusual postures in sleep or during travel, surgery or trauma, prolonged immobilization, pregnancy or puerperium, thrombocytosis, polycythaemia, diabetes, obesity, oral contraceptive pills, smoking, hormone replacement therapies, dyslipidaemia, atherosclerosis, congestive cardiac failure and malignancies [35,36] should be routinely monitored. In majority of the cerebral venous thrombosis patients, lifestyle issues and nutritional deficiencies such as folic acid, vitamin B6 and vitamin B12 deficiencies which are the commonest causes of hyper-homocystenemia, play a more important role in the pathogenesis of Cerebral venous thrombosis than any other inherited factors.[37]

Homocysteine (Hcy)

Homocysteine, a sulfur containing amino acid, was first obtained in 1933 from the urinary bladder stones by Vincent du Vigneaud.[38] Ever since, it has been under a lot of consideration and research. The chemical properties of Homocysteine were similar to cysteine and hence it was named as homocysteine. Heating of the amino acid methionine along with sulphuric acid has resulted in the formation of this amino acid. Vincent du Vigneaud has been awarded with the Nobel Prize in Chemistry in the year 1955, for his work on biochemically important sulphur compounds and most importantly for the synthesis of a polypeptide hormone for the first time.[39]

Hyperhomocysteinaemia (HHcy)

Increased circulating levels of Homocysteine or Hyper-Homocystenemia is one of the modifiable risk factors for stroke.[16,31] One study from Malaysia showed that moderate Hyper-Homocystenemia was an independent risk factor for stroke in 30% of the ischemic stroke patients.[40] Various epidemiological studies have stated that even milder cases of Hyper-Homocystenemia is related to venous thromboembolism and occlusive arterial vascular disease.[41-44] Limited knowledge regarding the role of homocysteine in Cerebral venous thrombosis is available. One study has revealed that higher plasma concentrations of homocysteine and lower serum folate levels were correlated with an increased risk of Cerebral venous thrombosis in lower socioeconomic groups and people with poor nutritional status.[45]

Pathogenesis Of Hyper-Homocystenemia

Homocysteine is produced by the protein breakdown during metabolism of methionine when it is converted to cysteine. There are 2 pathways of Homocysteine metabolism. (Figure 1) In case of excessive methionine, Homocysteine is diverted towards the transsulfuration pathway, then homocysteine is permanently sulfo-conjugated to cysteine by cystathionine B-synthatase enzyme with pyridoxine as cofactor. Homocysteine can be methylated through a conserving methionine

pathway, which necessitates the presence of vitamin B12 cofactor, methionine synthase enzyme and methyl tetrahydrofolate as co-substrate. On the other hand, the methionine-conserving pathway requires methyl tetrahydrofolate reductase (MTHFR) and folic acid. Serum Homocysteine levels are inversely proportional to serum folic acid levels, whereas plasma levels of vitamin B6 and vitamin B12 are weakly correlated with the plasma Homocysteine levels.

Thus, deficiencies of any of the folic acid or co factors may cause Hyper-Homocystenemia to some extent. Homocysteine is lethal to the endothelium of vessels which results in the oxidation of LDL cholesterol and enhance thrombosis. [8,39]

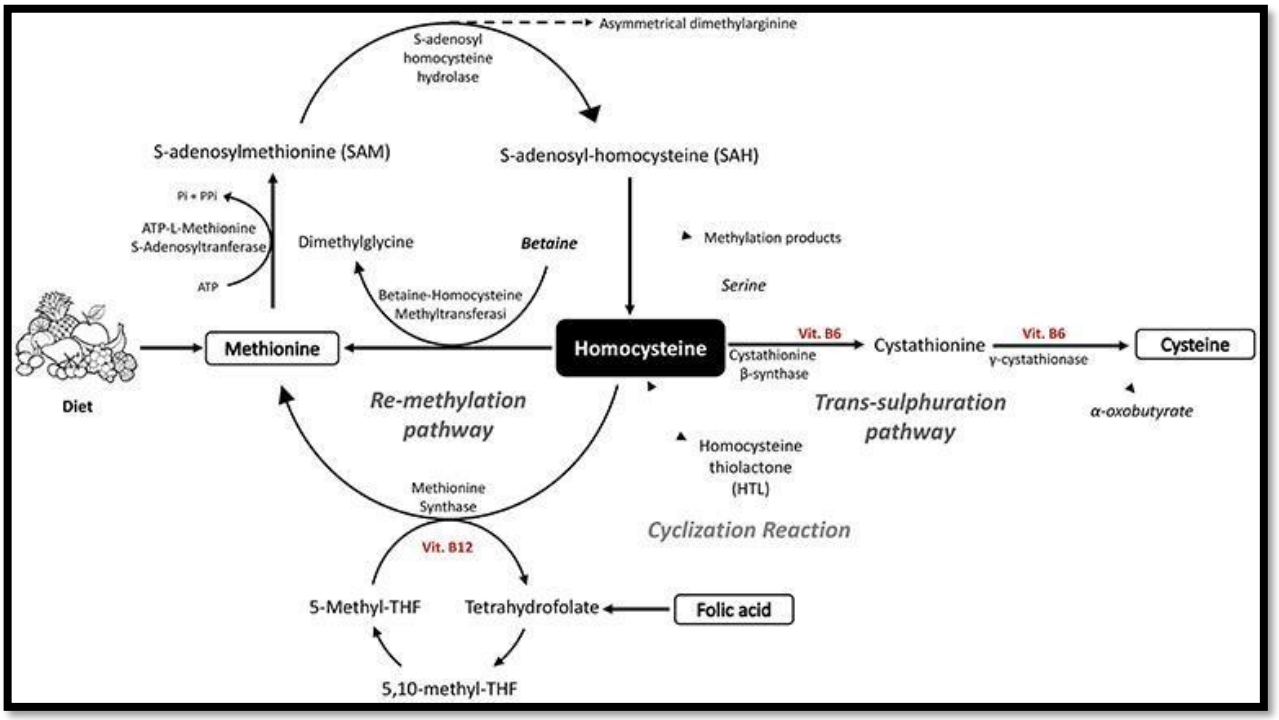


Figure : Homocysteine Metabolism [46]

Vitamin B12

Vitamin B12 (cobalamine), is a water-soluble vitamin. It is the largest and structurally most complicated vitamin, which comprises of a class of chemically related compounds known as vitamers. All the vitamers display physiological activity. It contains the biochemically rare element cobalt (Co) situated in the center of a corrin ring.[8,16] On an average, total body reserve of vitamin B12 is 3–5 mg, which is majorly present in liver.[47] Initially, it is bounded to intrinsic factor produced by the gastric parietal cells present within the duodenum and jejunum, and later it is absorbed in the terminal part of the ileum.[48] Hence even in the absence of vitamin B12 in the regular diet, the vitamin B12 stores can provide sufficient amount for approximately 5–10 years till the vitamin B12 deficiency manifests clinically.[15] Vitamin B12 levels are classified as Normal (190-900 pg/ml), mild deficiency (100-189 pg/ml) and severe deficiency (<100pg/ml).[8]

Vitamin B12 deficiency

Vitamin B12 deficiency is often caused as a result of malabsorption due to conditions such as celiac disease, autoimmune gastritis (pernicious anemia), inflammatory bowel disease, gastric bypass, ileal resection and surgical gastrectomy. It may also occur because of nutritional habits such as strict vegans, breastfed infants born to vegan mothers with decreased dietary intake of animal products, nitrous oxide abuse, diphyllobothrium latum infection, pancreatic insufficiency, interference of drugs like proton pump inhibitors, metformin, drug affected purine and pyrimidine synthesis, inherited disorders which affects intrinsic factor as well as other inherited disorders like methylmalonic acidemia and transcobalamin II deficiency abuse.[15,49,50]

Vitamin B12 and Homocysteine

During the period of 1940, extensive research was done to find the crucial factor in the liver extracts which averted the occurrence of pernicious anemia. This exploration revealed that folate and vitamin B12 both helps in preventing megaloblastic anemia, however, only vitamin B12 can prevent the neurological complications.[51] It is a well-established fact that both vitamin B12 and folate works together to regenerate methionine from Homocysteine. When the conversion of Homocysteine to methionine slows down due to deficiency of vitamin B12, folate or both, Homocysteine starts accumulating within the blood suggesting an inefficient metabolism of amino acids. This causes certain adverse effects including increased risk of some cancers, dementia, and cardiovascular diseases due to thickening of the lining epithelium of blood vessels.[15] As previously reported [52], Methionine synthase is a vitamin-B12-dependent enzyme which catalyses the folic acid's donation of a methyl group across the methylenetetrahydrofolate reductase (MTHFR). Increased serum levels of Homocysteine can occur due to deficiency of cobalamin (vitamin B12), conversely, the serum concentration of Homocysteine falls when the concentration of vitamin B12 rises. [8,15] In human beings, even mild and moderate Hyper-Homocystenemia are associated with mutations of MTHFR genes.[15]

Nagaraja D et al [53] **(2008)** did a case-control study to investigate the relation between Homocysteine (Hcy), cobalamin and folate levels in patients with puerperal Cerebral venous thrombosis. Study included 60 women with puerperal Cerebral venous thrombosis and 64 healthy puerperal control patients. The results showed that adjusted odds ratio for the risk of puerperal Cerebral venous thrombosis with Hyper-Homocystenemia (>90th percentile) was 10.8, while lower levels of cobalamin and vitamin B9 did not increase the risk for Cerebral venous thrombosis in pregnancy. Inverse correlation was found between folate and total homocysteine. The study concluded that Hyper-Homocystenemia is linked with Cerebral venous thrombosis in pregnancy

affecting women in India and low vitamin b9 levels significantly contributed to Hyper-Homocystenemia.

Taheraghdam AA et al [29] **(2016)** conducted a cross-sectional case-control study to analyse the risk of low folic acid, low vitamin B12 and Hyper-Homocystenemia(HHcys) for Cerebral venous thrombosis. The study comprised of 24 patients suffering from Cerebral venous thrombosis and 36 healthy controls. The deficient levels of folic acid and vitamin B12 considered for the study was less than 10th percentile of folic acid and vitamin B12 level and HHcys was considered as more than 90th percentile of homocysteine of the control group. The authors observed that total homocysteine (tHcys) levels were significantly higher in the patient group as compared to the control group. Also, the level of vitamin B12 were lower in the study group. Hyper-Homocystenemia and low vitamin B12 levels were significantly more prevalent in the Cerebral venous thrombosis patients than controls. Hyper-Homocystenemia and low vitamin B12 were found as significant independent risk factors for Cerebral venous thrombosis, but no significant correlation was found between low folic acid and risk of Cerebral venous thrombosis. A statistically significant negative correlation was observed between the levels of total homocysteine and vitamin B12 levels. Thus, they concluded that Hyper-Homocystenemia and low vitamin B12 levels were associated with the high risk of for Cerebral venous thrombosis.

Harale M et al [30] **(2019)** did a study to investigate Cerebral venous thrombosis patients and to find the correlation between raised levels of homocysteine and cerebral venous thrombosis. The study comprised of 50 study patients who were diagnosed for Cerebral venous thrombosis by imaging of brain and 50 healthy individuals who constituted the control group. Serum homocysteine levels and vitamin B12 levels were done in all the patients. The results showed that the incidence of Hyper-Homocystenemia in their study was 70%. The homocysteine levels of the patient group were higher than that of the control group, whereas the vitamin B12 levels of patient group are lower than that of control group. Hyper-Homocystenemia was observed in majority of

male patients in the age group of 30-40 year, while most of the females were in the 50–60-year age group. On comparing the homocysteine and B12 values, they found that when B12 value is lower, homocysteine level tends to be higher, but, if homocysteine level is high, B12 level is not necessarily low. Thus, the study concluded that, Hyper-Homocystenemia is associated with Cerebral venous thrombosis and that lower B12 levels are always associated with Hyper-Homocystenemia but Hyper-Homocystenemia may or may not be associated with low B12 level.

Markisic M et al[54] **(2017)** did a non-interventional prospective clinical study to evaluate the relationship between acute ischaemic stroke (IS) early functional outcome and serum levels of homocysteine, vitamin B12 and D. Laboratory investigations and functional assessment were performed at the time of admission and three and six months after stroke. Barthel index (BI), Modified Rankin Scale (mRS), and NIHSS scale were assessed in all the patients by expert examiner blinded to laboratory data. None of the patients receive treatment which might alter the laboratory results. The authors found that National institute of health (NIHSS) score at admission was correlated with homocysteine, B12 and vitamin D levels. A positive correlation was found between with vitamin B12 levels for Barthel index at 3 and 6 months and modified ranking scale at 6 months. However, the Barthel index and modified ranking scale scores were not significantly related with homocysteine and vitamin D3 levels at 3 and 6 months. They concluded that higher plasma vitamin B12 levels were associated with better functional outcome at follow-up.

Kalita J et al [56] **(2020)** did a study to investigate the relationship of homocysteine (Hcy) with vitamin B12, folic acid and methyl tetrahydrofolate reductase (*MTHFR*) mutation in the patients with Cerebral Venous Sinus Thrombosis (CVT) and to compare the severity and outcome of patients clinico-radiologically, with and without Hyper-Homocystenemia in 96 patients. All the patients were evaluated for prothrombotic conditions including homocysteine, vitamin B12, folic acid and *MTHFR* 677C→T mutation. The results of the study showed that 73% of the patients had

risk factors. Hyper-Homocystenemia was present in 52.1% patients, protein S deficiency was seen in 47.8% patients, protein C deficiency in 19.4%, *MTHFR* 677C→T mutation in 30.7%, antinuclear antibody in 11% and Factor V Leiden mutation in 2% of the patients. 32% patients with Hyper-Homocystenemia had no other causes of thrombosis.whereas 22% had either vitamin B12 or folic acid deficiency only. The patients with Hyper-Homocystenemia more frequently had vitamin B12 deficiency (70 vs. 13%), *MTHFR* 677C→T mutation (47.5 vs. 9.1%) and superior sagittal sinus thrombosis (78 vs. 56.5%) than normal Hcy group.

The clinico-radiological severity and outcome were similar. The authors concluded that Hyper-Homocystenemia was a vital correctable risk factor in Cerebral venous thrombosis patients and most of the patients had either vitamin B12 deficiency or *MTHFR* mutation

Kamran S et al [8] **(2021)** conducted a study to evaluate the correlation between Cerebral Venous Sinus Thrombosis and Serum Homocysteine levels in 76 patients suffering from Cerebral venous thrombosis. Fasting serum homocysteine levels and serum B12 levels were analysed in each study patient. Based on the serum homocysteine levels, the patients were grouped into 4 categories as Normal Level, Mild Hyper-homocystenemia, Moderate and Severe Hyper-homocystenemia.

Depending on serum B12 levels, patients were divided into 4 groups as Severe Deficiency, Mild Deficiency, Normal range and High levels. The results of this study have shown that homocysteine levels were significantly higher in Cerebral venous thrombosis patients, but no correlation was observed between Serum B12 levels and Cerebral venous thrombosis. Thus, the study concluded that Hyper-Homocystenemia could be a risk factor for Cerebral Venous Sinus Thrombosis.

Sohan B et al [31] **(2022)** did a study to investigate the co-relation of cerebral venous sinus thrombosis with vitamin B12 and homocysteine levels in a tertiary care center. The study comprised of total 62 patients, out of which, maximum patients were in the age group of 31- 40 years followed by 19-30 years and 66.13% were male and 33.87% were female. Most commonly observed signs and symptoms were headache, followed by visual disturbance, nausea/vomiting, hemiparesis, unconscious, seizure and speech disturbance. The authors observed that Hyper-Homocystenemia(HHCy) was present in 58.06% of the patients and it was significantly associated with the Motor deficit, GCS score, Cranial nerve involvement, Mechanical ventilator, Seizure, Sinus (types) involvement and Outcome. However, they did not find any significant correlation between Vitamin B12 deficiency and Motor deficit, GCS score, Cranial nerve involvement, Mechanical ventilator, Seizure, Sinus (types) involvement and Outcome. Thus, they concluded that serum Hyper-Homocystenemia is a risk factor for the development of Cerebral Venous Sinus Thrombosis.

Kapur V et al [55] **(2019)** reported a case of cerebral venous thrombosis secondary to Hyper-Homocystenemia which was caused due to vitamin B12 deficiency in a 32-year-old Indo-Aryan male who was a strict vegetarian. The presenting signs and symptoms were frequent vomiting, moderate to severe headache and giddiness since 5 days. He also reported weakness of the right side of the body along with altered sensorium since last 24. Detailed laboratory investigations, especially coagulation work up was suggestive of Hyper-Homocystenemia which was due to vitamin B12 deficiency. Thus, the authors concluded that Hyper-Homocystenemia is associated with an enhanced risk of Cerebral venous thrombosis.

MATERIALS AND METHOD

STUDY DESIGN:

This was the Hospital based prospective, observational study, conducted on patients Cerebral venous thrombosis who are admitted in BLDE (DU)'s B.M. Patil Medical College and Hospital, Vijayapura.

STUDY DURATION AND PLACE:

The study was conducted period from January 2021 to July 2022. (18 months). It was conducted at one of Tertiary care hospital in BLDE (DU)'s B.M. Patil Medical College and Hospital, Vijayapura.

STUDY POPULATION:

All the patients admitted Cerebral venous thrombosis in BLDE (DU)'s B.M. Patil Medical College and Hospital, Vijayapura, during the study period.

Sample Size:

With anticipated Prevalence of high levels of homocysteine in CVT patients 70.7% (ref), the study would require a sample size of 55 patients with a 95% level of confidence and 12% absolute precision. Formula used

$$N = \frac{z^2 P\ (1-p)}{ME^2}$$

Where Z = Z statistic at α level of significance

ME^2 = Marginal Error

P = Proportion rate = 70.7%

Q = 100-P =29.3%

Patients Selection: Patients were selected by using simple random sampling method admitted for Cerebral venous thrombosis in the hospital.

INCLUSION CRITERIA:

1) Clinical history and neurological examination
2) By the presence of radiological evidence of cortical venous sinus thrombosis.

EXCLUSION CRITERIA:

1. Patients who are on Drugs causing vitamin B12 deficiency
2. Patients on vitamin B 12 supplements
3. Patients on Drugs or health conditions interfering with homocysteine metabolism

ETHICAL COMMITTEE APPROVAL:

The present study was approved by institutional ethics committee of our tertiary care in BLDE (DU)'s B.M. Patil Medical College and Hospital, Vijayapura committee.

METHODS:

Each patient had a detailed clinical history and complete neurological examination. Fasting serum homocysteine and serum B12 levels were measured in each subject.

Evaluation of homocysteine is done by

Machine-Eurolyser smart 700/340

Method-Liquid chromatography-tandem mass spectrometry

Specimen Type-Plasma EDTA

Specimen Volume-1 mL

Container -Plastic vial (Green top)

The patients were categorised into 4 groups based on their serum homocysteine levels: Normal Level, Mild Hyper-Homocystenemia, Moderate Hyper-Homocystenemia, and Severe Hyper-Homocystenemia.

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

Evaluation of Vitamin B12 is done by

Machine Name-Beckman Coulter Access 2

Specimen Type-Serum

Specimen Volume-0.6 mL

Method Name-Immuno enzymatic assay

The patients were separated into 4 groups based on their serum B12 levels: Severe Deficiency, Mild Deficiency, Normal range, and High levels.

1. Severe Deficiency: <100 pg/ml
2. Mild Deficiency: 100-189 pg/ml
3. Normal Range: 190-900 pg/ml
4. High levels: >900 pg/ml

STATISTICAL ANALYSIS:

Quantitative data were provided by mean and standard deviation for analysis, while qualitative data were presented with proportion and percentages. Collected data were imported into Microsoft Excel 2016 for further analysis. Chi-square tests were used to evaluate qualitative analyses (association or percentage difference), whereas Man-Whitney tests were used to evaluate quantitative data (mean difference) when the data were not normally distributed. To determine the link between variables, the Pearson correlation coefficient was discovered. P values of 0.05 or below were regarded as statistically significant. Version 25 of SPSS software was utilised for the statistical analysis.

RESULTS

Table 1: Gender distribution among the study population

Gender	Frequency	Percent
Male	29	52.7
Female	26	47.3
Total	55	100

Study found that majority of males were suffered with cerebral venous thrombosis (CVTS) compared to female.

Figure 1: Gender distribution among the study population

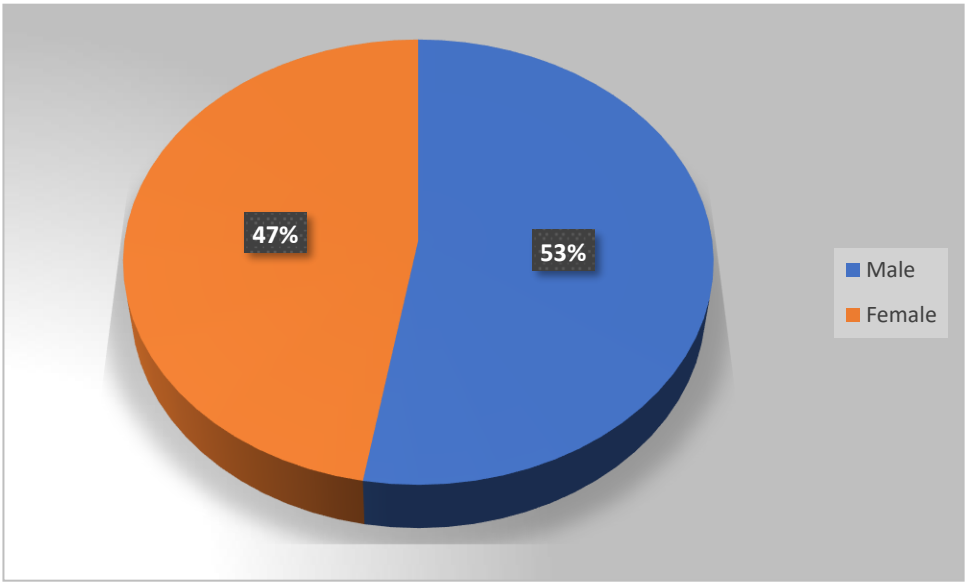


Table 2: Age distribution among the study population

Age	Frequency	Percent
< 20 Years	2	3.6
21 - 40 Years	29	52.7
41 - 60 Years	12	21.8
61 - 80 Years	12	21.8
Total	55	100

Among the all patients with CVTS majority of the patients from age groups of 20-40 years, followed by each of 21.8% from 40-60 years and 61-80 years, there were only 2 patients from age group < 20 years, both patients had age of 18 years.

Figure 2: Age distribution among the study population

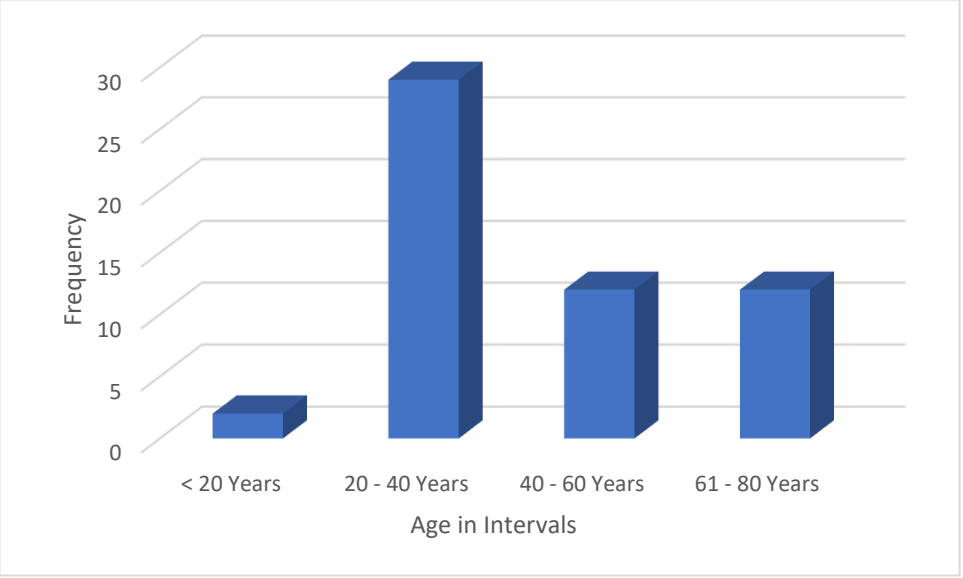


Table 3: Distribution of Comorbid Condition among the study population

Comorbidity	Frequency	Percent
Diabetes Mellitus	1	1.8
Hypertension	1	1.8
Hypertension, Diabetes Mellitus	2	3.6
HTN, Epilepsy	2	3.6
HTN, DM, IHD	1	1.8
Epilepsy, Polio	1	1.8
Nil	47	85.5
Total	55	100

We have observed only 8 patients with some comorbidities like HNT, DM, Epilepsy etc shown in the above table, out of that hypertension and diabetes mellitus was more common we have observed.

Figure 3: Distribution of Comorbid Condition among the study population

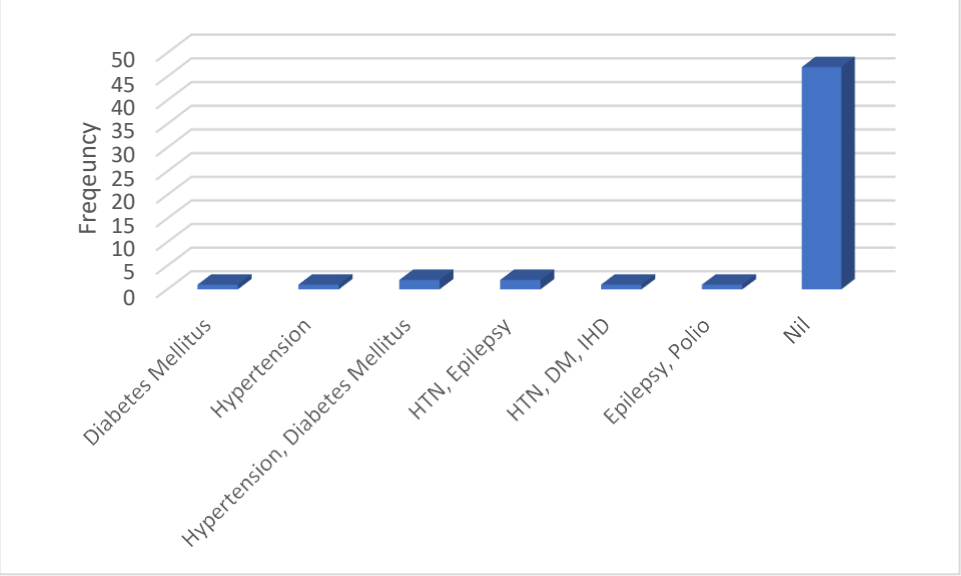


Table 4: Distribution of Location of thrombosis among the study population

Location of Thrombosis	Frequency	Percentage
Left Occipital and temporal regions	7	12.7
Right Frontal and Parietal	6	10.9
Left frontal temporal parietal	5	9.1
Left high parietal	5	9.1
Left Temporal	5	9.1
Right Frontol	3	5.5
Left Occipital	3	5.5
Left anterior frontal Lobe	2	3.6
Left frontal parietal	2	3.6
Bellow Cerebral Hemisphere and cerebral vermis	2	3.6
Below Frontal parietal	2	3.6
Right Frontal Lobe haemorrhage	2	3.6
Right Side of Mid Brain	2	3.6
Left Parietal Temporal	2	3.6
Anterior part superior sagittal sinus	1	1.8
Bellow Frontal Parietal region	1	1.8
Left Frontal parietal and Capsule	1	1.8
Left Frontal parietal temporal	1	1.8
Left Parietal	1	1.8
Left parietal occipital Temporal Lobos	1	1.8
Straight Sinus	1	1.8

Figure 4: Distribution of thrombosis among the study population

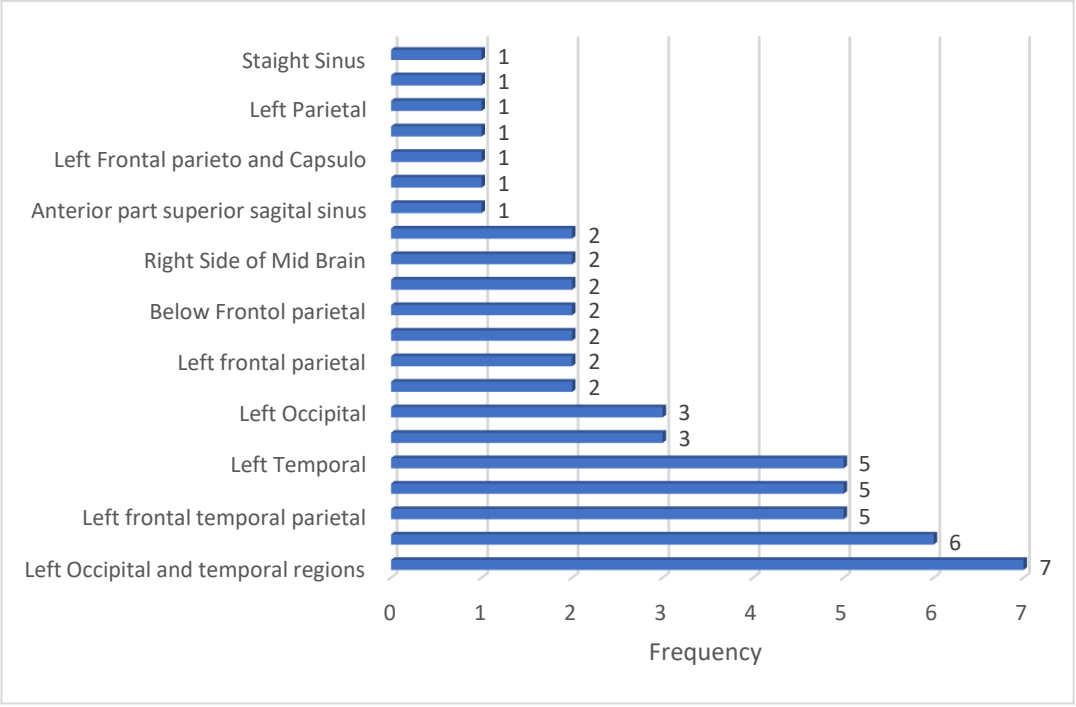


Table 5: Distribution of sinus involvement among the study population

Sinus Involvement	Frequency	Percentage
Superior Sagittal Sinus	13	23.6
Left Sigmoid & transverse Sinus	9	16.4
Left transverse and internal juggler	5	9.1
Diffuse Venous Sinus	5	9.1
Internal cerebral veins	4	7.3
Left Transverse Sinus	4	7.3
Superior Sagittal and right transverse sinus	3	5.5
Left Sagittal transverse vein	2	3.6
Left Transverse Sinus and Sigmoid	2	3.6
Straight sinus, left transverse, sigmoid sinus	1	1.8
Superior Sagittal & Left transverse Sinus	1	1.8
Superior Sagittal lateral transverse	1	1.8
Superior Sagittal Sigmoid Sinus	1	1.8
Superior Sagittal Sinus, Lateral Transverse, & Sigmoid	1	1.8
Superior Sagittal Sinus, transverse & sigmoid	1	1.8
Thrombosis of veins of trocand	1	1.8
transverse sigmoid and internal juggler	1	1.8

Figure 5: Distribution of sinus involvement among the study population

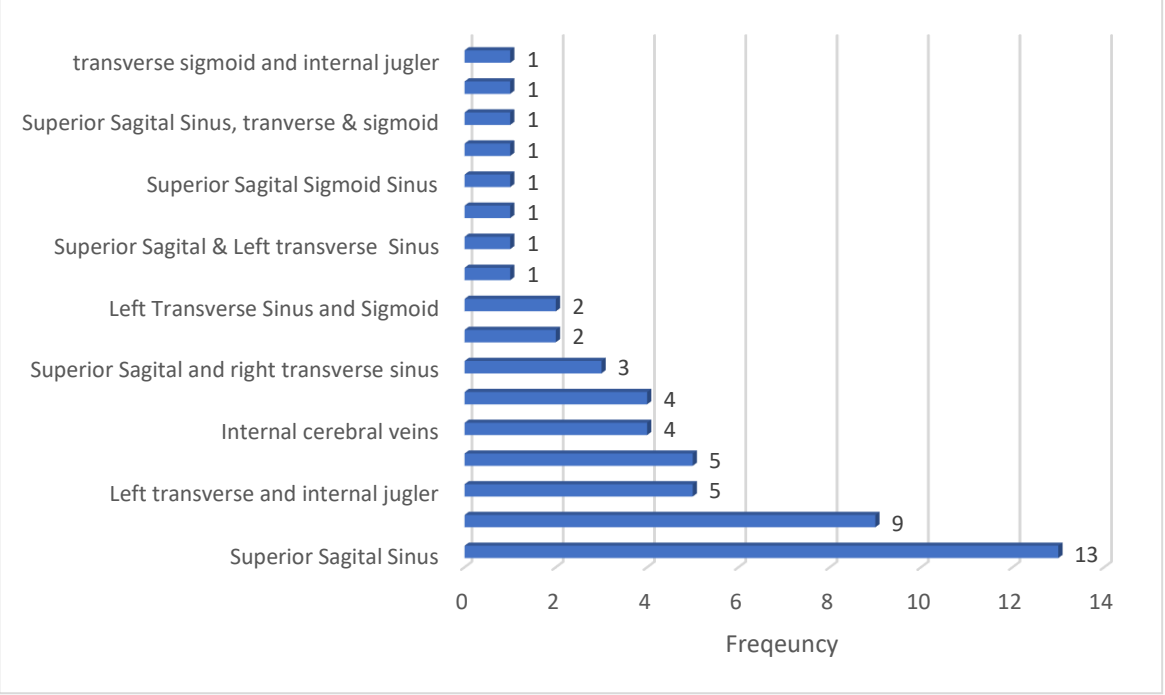


Table 6: Distribution of Symptoms among the study population

Symptoms	Frequency	Percentage
Headache	21	38.2
Vomiting	10	18.2
Weakness	10	18.2
Seizures	9	16.4
Giddiness	8	14.5
Fever	4	7.3
Altered Sensorium	4	7.3
Loss of Speech	4	7.3
Slured Speech	3	5.5
Blurring of vision	2	3.6
Others (Fall, Numbness, No Response, Involuntary Movement)	12	21.8

Among the all-patients maximum patients were observed the symptoms of headache, vomiting, weakness seizures and giddiness, only 2 patients observed with blurring of vision and 4 patients found with loss of speech.

Figure 6: Distribution of Symptoms among the study population

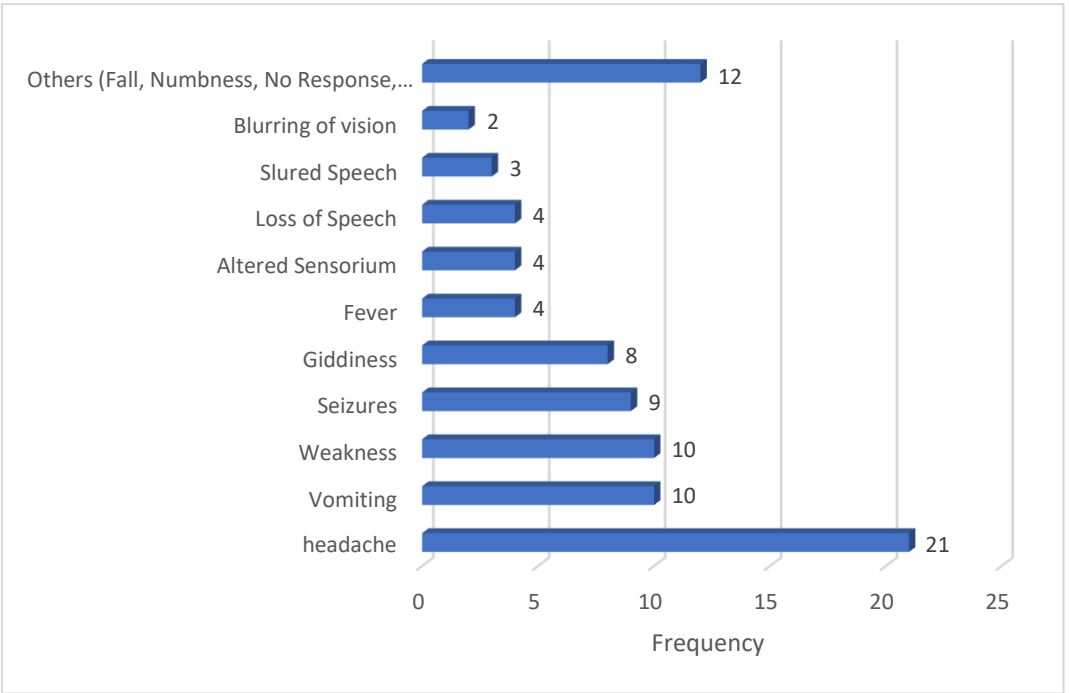


Table 7: Distribution of Homocysteine levels among the study population

Homocysteine Intervals	Frequency	Percent
4- 15 nmol/L. (Normal Level)	10	18.2
15 - 30 nmol/L. (Mild Hyper-homocystenemia)	22	40
30 - 100 nmol/L. (Moderate Hyper-homocystenemia)	19	34.5
> 100 nmol/L. (Severe Hyper-homocystenemia)	4	7.3
Total	55	100

Among all the patients 40% of the patients had homocysteine level was mild, followed by moderate level and normal level, we have found 4 patients with Severe Hyper-Homocystenemia

Figure 7: Distribution of Homocysteine levels among the study population

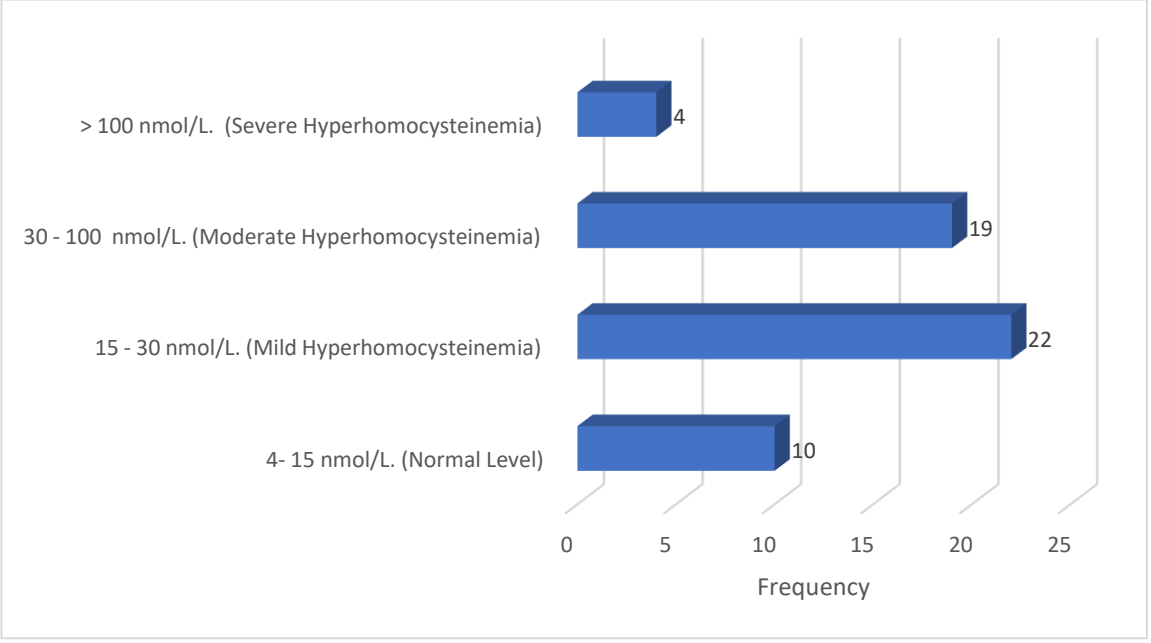


Table 8: Distribution of Vitamin B12 levels among the study population

Vitamin B12 Interval	Frequency	Percent
< 100 pg/ml (Severe Deficiency)	25	45.5
100-189 pg/ml (Mild Deficiency)	14	25.5
190-900 pg/ml (Normal Range)	16	30
Total	55	100

We have found that majority of patients observed with severe deficiency of vitamin B12, followed by normal. Also, we have observed 25.5% of the patients had there vitamin B12 mildly deficient.

Figure 8: Distribution of Vitamin B12 levels among the study population

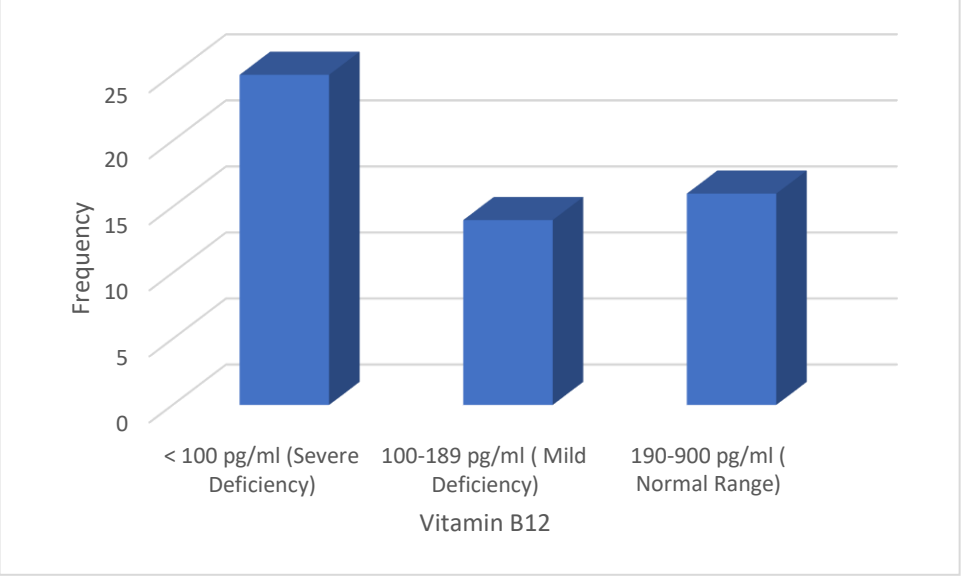


Table 9: Distribution of Hb levels among the study population

Hb Level	Frequency	Percent
< 10 gm/dL	9	16.4
10 - 15 gm/dL	38	69.1
> 15 gm/dL	8	14.5
Total	55	100

Study observed mean Hb level of the patients were in the normal range, only patients had Hb level was below 10 gm/dl, most of them were females.

Figure 9: Distribution of Hb levels among the study population

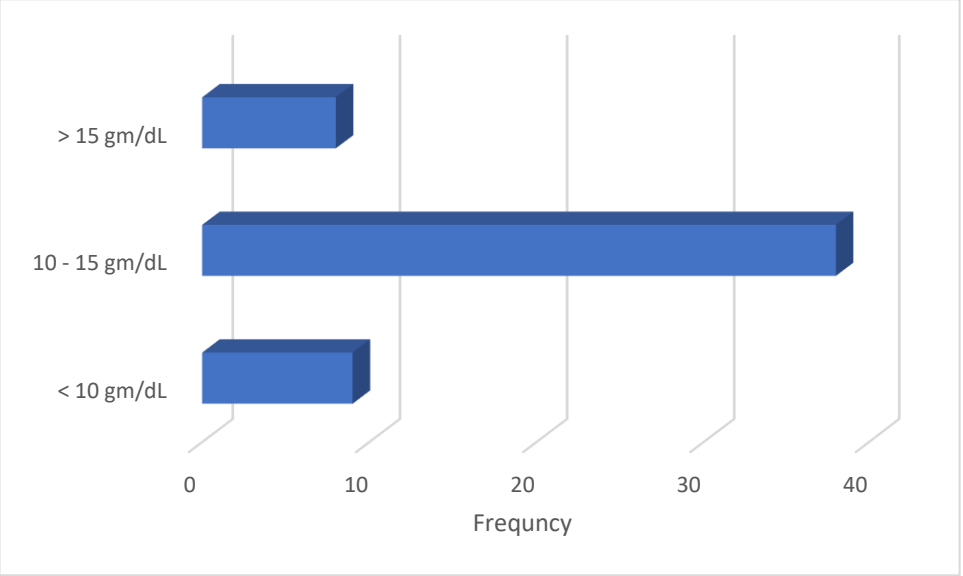


Table 10: Distribution of Platelets Count among the study population

Platelets Count	Frequency	Percent
< 1.5 lakhs per microliter	5	9.1
> 1.5 lakhs per microliter	50	90.9
Total	55	100

Except 5 patients all the patients had their platelets count was normal above 1.5lakhs per microliters.

Figure 10: Distribution of Platelets Count among the study population

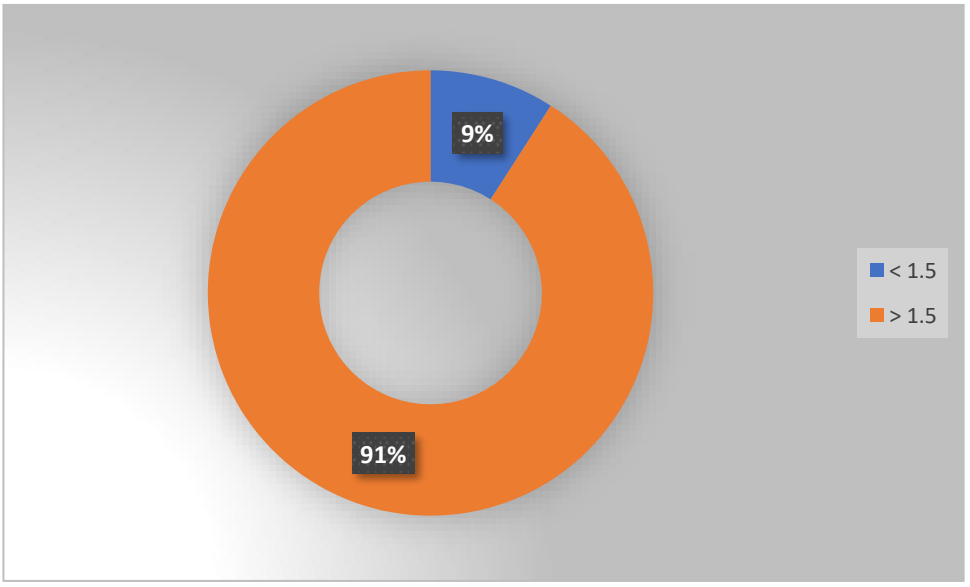


Table 11: Distribution of Glasgow Coma Scale among the study population

GCS Scale	Frequency	Percent
9-12	15	27.3
13 – 15	40	72.7
Total	55	100

We observed maximum patients had there GCS scale was more than 12, only 15 patients had there GCS level was moderate. But they were conscious.

Figure 11: Distribution of Glasgow Coma Scale among the study population

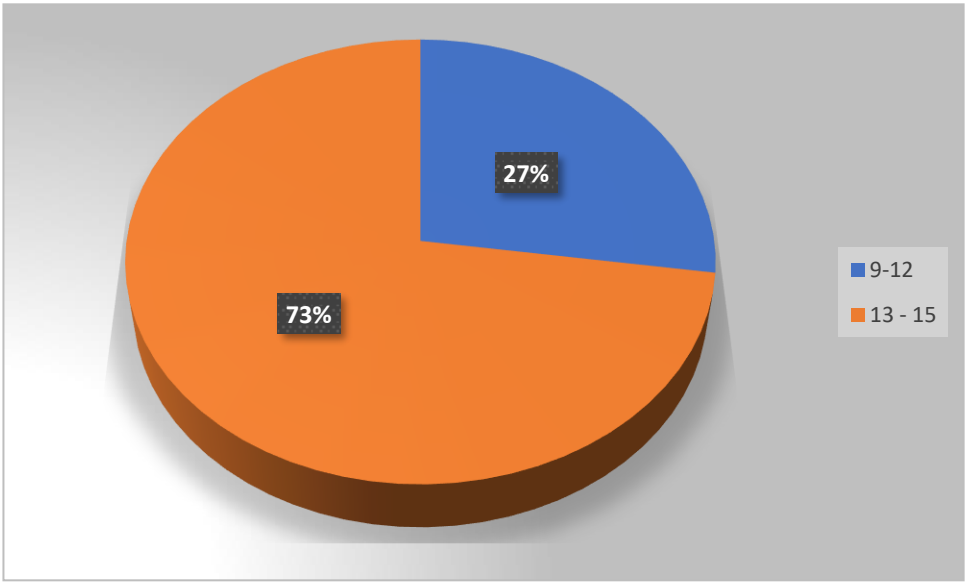


Table 12: Distribution of Homocysteine levels among gender.

Homocysteine Intervals	Sex		Total	Chi-square	P-value
	Male	Female			
4- 15 nmol/L. (Normal Level)	3(5.50%)	7(12.70%)	10(18.20%)	5.68	0.136
15 - 30 nmol/L. (Mild Hyper-homocystenemia)	12(21.80%)	10(18.20%)	22(40.0%)		
30 - 100 nmol/L. (Moderate Hyper-homocystenemia)	10(18.20%)	9(16.40%)	19(34.50%)		
> 100 nmol/L. (Severe Hyper-homocystenemia)	4(7.30%)	0(0%)	4(7.30%)		
Total	29(52.70%)	26(47.30%)	55(100%)		

Table showed that there was no statistically significant difference of homocysteine levels between male and females, it was comparable in both the groups.

Table 12: Distribution of Homocysteine levels among gender.

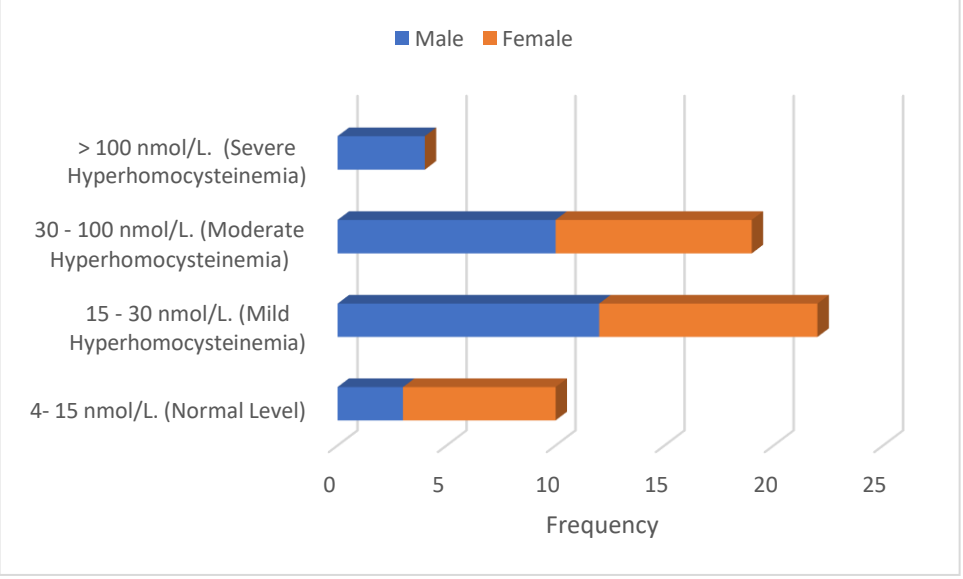


Table 13: Distribution of vitamin B12 levels among gender.

Vitamin B12 Interval	Sex		Total	Chi-square	P-value
	Male	Female			
< 100 pg/ml (Severe Deficiency)	15(27.30%)	10(18.20%)	25(45.50%)	2.12	0.345
100-189 pg/ml (Mild Deficiency)	8(14.50%)	6(10.90%)	14(25.50%)		
190-900 pg/ml (Normal Range)	6(10.90%)	10(18.20%)	16(29.10%)		
Total	29(52.70%)	26(47.30%)	55(100%)		

Male and female vitamin B12 levels were equivalent in both groups and did not differ significantly from one another.

Figure 13: Distribution of Vitamin B12 levels among gender.

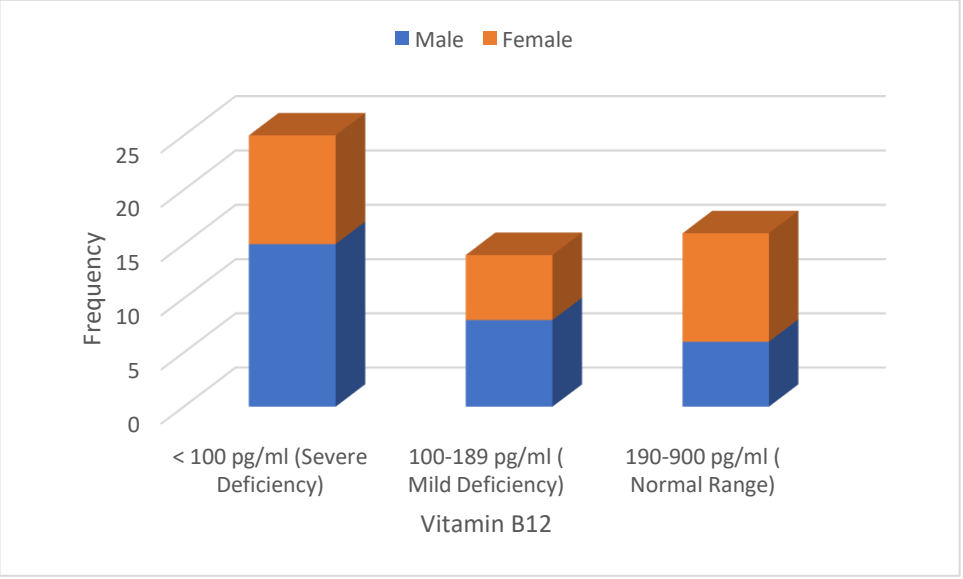


Table 14: Age distribution among in gender

Age	Sex		Total	Chi-square	P-value
	Male	Female			
< 20 Years	0(0%)	2(3.6%)	2(3.60%)	3.82	0.302
21 - 40 Years	16(29.10%)	13(23.60%)	29(52.70%)		
41 - 60 Years	8(14.50%)	4(7.30%)	12(21.80%)		
61 - 80 Years	5(9.10%)	7(12.70%)	12(21.80%)		
Total	29(52.70%)	26(47.30%)	55(100%)		

We observed comparable age group between the male and females

Figure 14: Age distribution among in gender

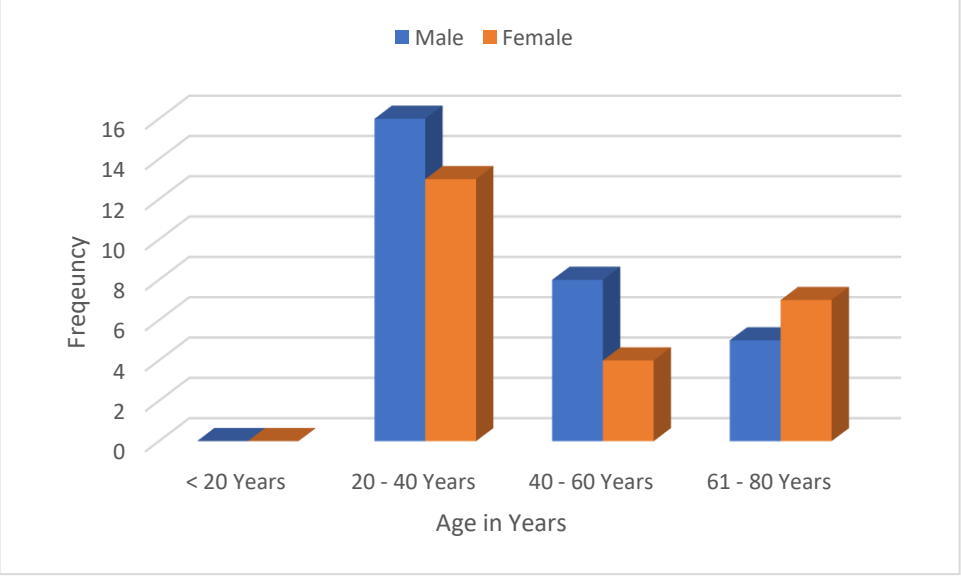


Table 15: Homocysteine distribution among age groups

Age	Homocysteine Intervals				Total	Chi-square	P-value
	4- 15 nmol/L	15 - 30 nmol/L.	30 - 100 nmol/L	> 100 nmol/L.			
< 20 Years	0(0%)	1(1.80%)	1(1.80%)	0(0%)	2(3.60%)	6.71	0.704
21 - 40 Years	5(9.10%)	12(21.80%)	10(18.20%)	2(3.60%)	29(52.70%)		
41 - 60 Years	1(1.80%)	6(10.90%)	5(9.10%)	0(0%)	12(21.80%)		
61 - 80 Years	4(7.30%)	3(5.50%)	3(5.50%)	2(3.60%)	12(21.80%)		
Total	10(18.20%)	22(40.0%)	19(34.50%)	4(7.30%)	55(100%)		

Distribution of Homocysteine levels among the different age groups was not statistically significant, it was comparable in al the age groups.

Figure 15: Homocysteine distribution among age groups

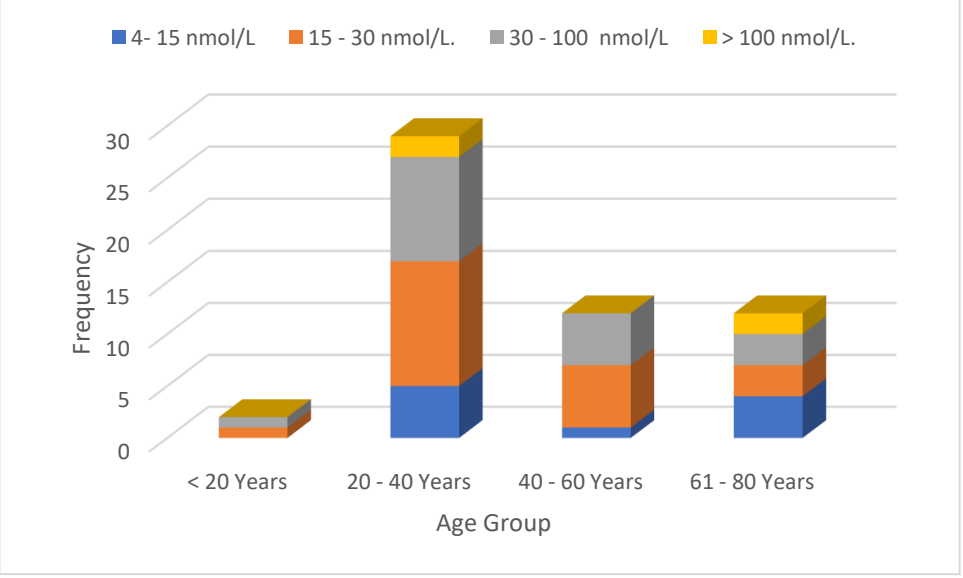


Table 16: Vitamin B12 distribution among age groups

Age	Vitamin B12			Total	Chi-square	P-value
	< 100 pg/ml	100-189 pg/ml	190-900 pg/ml			
< 20 Years	1(1.80%)	0(0%)	1(1.80%)	2(3.60%)	2.34	0.96
21 - 40 Years	13(23.60%)	7(12.70%)	9(16.40%)	29(52.70%)		
41 - 60 Years	6(10.90%)	4(7.30%)	2(3.60%)	12(21.80%)		
61 - 80 Years	5(9.10%)	3(5.50%)	4(7.30%)	12(21.80%)		
Total	25(45.50%)	14(25.50%)	16(29.10%)	55(100%)		

Distribution of Vitamin B12 levels among the different age groups was not statistically significant, it was comparable in al the age groups.

Figure 16: Vitamin B12 distribution among age groups

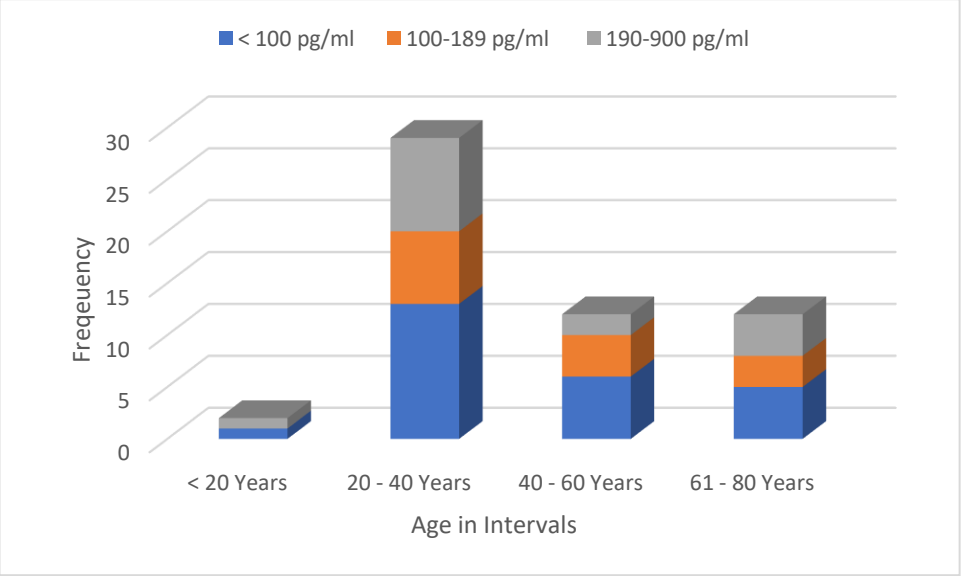


Table 17: Vitamin B12 distribution among Homocysteine levels

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%)		

**P-value<0.001 statistically highly significant at 5% level of Significance.

We have observed the proportion of vitamin B12 among various homocysteine levels varied statistically significantly. Maximum vitamin B12 deficient patients were observed in mild to moderate levels of Homocysteine.

Figure 17: Vitamin B12 distribution among Homocysteine levels

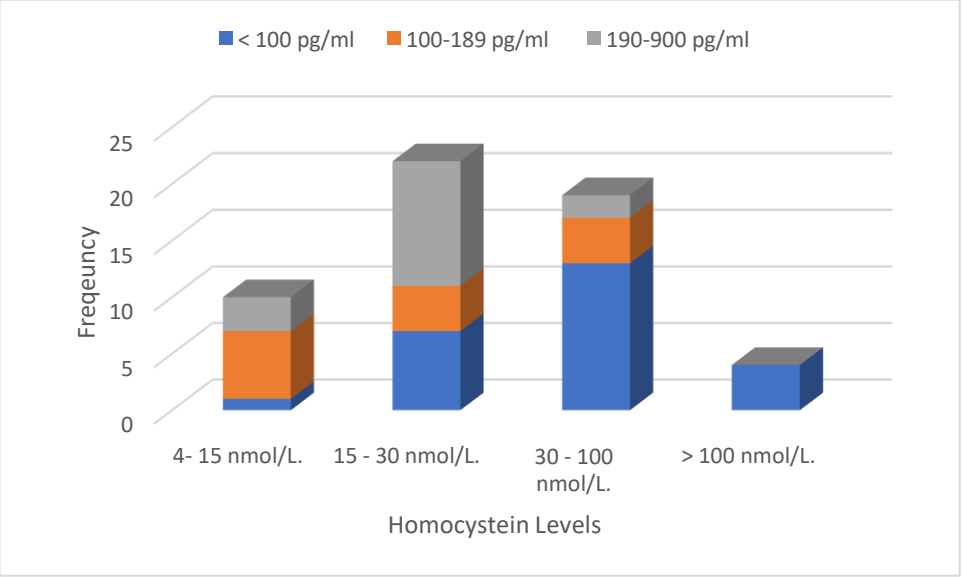


Table 18: Lab Parameters between raised and normal Homocysteine

Lab Parameters	Homocysteine	N	Mean	Std. Deviation	t-test	P-value
Hb Level	Normal	10	12.67	1.9184	-0.086	0.932
	Raised	45	12.731	2.4305		
MCV	Normal	10	83.48	8.6882	0.292	0.773
	Raised	45	82.431	15.5113		
MCH	Normal	10	26.56	3.2908	-1.716	0.106
	Raised	45	28.624	4.049		
Platelets Count	Normal	10	2.885	1.23766	0.127	0.901
	Raised	45	2.8296	1.31804		
ESR	Normal	10	31.1	16.128	1.767	0.102
	Raised	45	21.33	14.299		

We have found no laboratory parameters were significant different, between raised and normal level of homocysteine.

Table 19: Lab Parameters between raised and normal Homocysteine

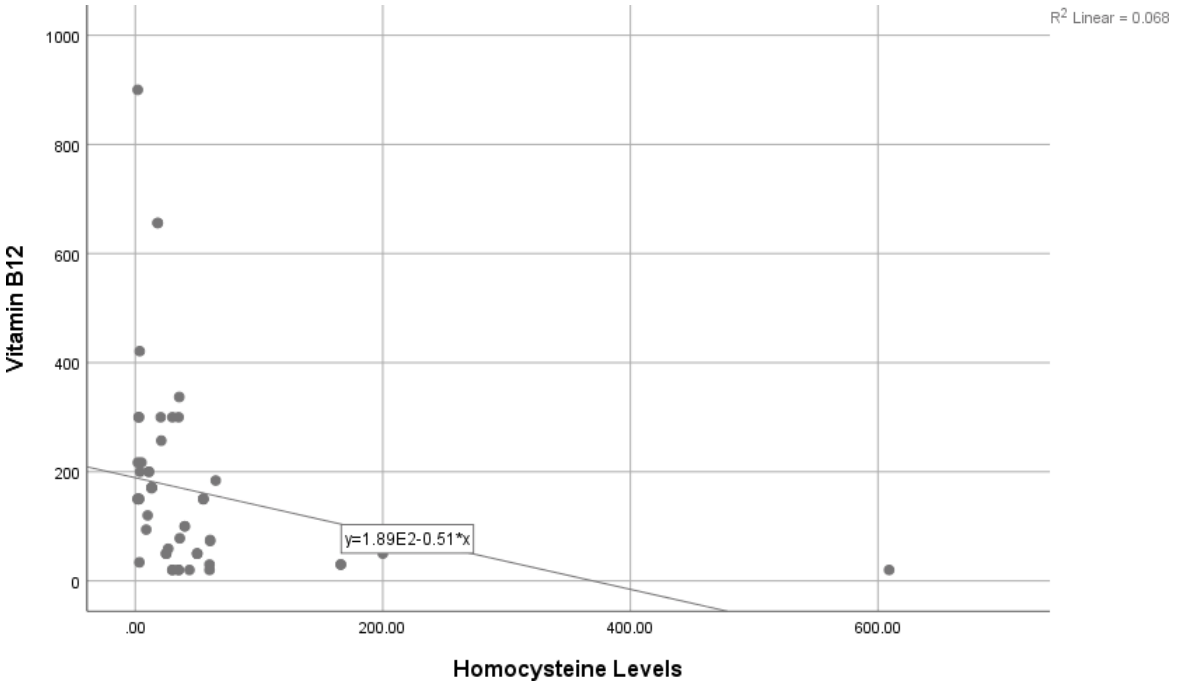
Parameters	Homocysteine	N	Mean	Std. Deviation	t-test	P-value
GCS Score	Normal	10	12.5	2.635	-1.963	0.055
	Raised	45	13.93	1.959		
vitaminB12	Normal	10	166.4	37.355	0.0008	0.982
	Raised	45	166.16	189.395		
Prothrombin time	Normal	10	13.2	2.1797	0.03	0.976
	Raised	45	13.173	3.6173		

Table 20: Correlation between Homocysteine level and other parameters.

Homocysteine levels	vitaminB12	GCS Score	Prothrombin time	Platelets Count	HbLevel
Pearson Correlation	-0.26	0.14	-0.038	-0.06	0.027
Significance	0.055	0.309	0.783	0.662	0.846
N	55	55	55	55	55

Correlation between Homocysteine level and other parameters like Vitamin B12, GCS score, Prothrombin Time, Platelets counts and Hb level was not statistically correlated. Only we found Homocysteine level and Vitamin B12 level was significant negatively correlated at 10% level of significance.

Figure 18: Correlation between Homocysteine Vitamin B12.



DISCUSSION

Homocysteine is an alpha amino acid that largely derives from methionine, a by-product of the metabolism of proteins. Homocysteine is normally transformed to cystathione to cysteine through the transsulfuration pathway which is then eliminated by urinary system. In this route, pyridoxine is needed as a cofactor. Another process, known as the remethylation pathway, uses methylene tetrahydrofolate reductase (from the metabolism of folate), which aids methionine synthetase in converting homocysteine back to methionine. Hyper-Homocystenemia results from any disorder in this route since vitamin B12 is a cofactor in this process. Numerous factors can occur alone or in combination to predispose to cerebral venous thrombosis. There are several disorders that are well-known, including sinusitis, trauma, surgery, hypercoagulable states (such as antiphospholipid syndrome, protein C and protein S deficiency, and anti-thrombin deficiency), vasculitis, pregnancy, puberty, use of OCPs, nephrotic syndrome, malignancy, etc. It is challenging to make a diagnosis of cerebral venous thrombosis because patients with this condition frequently experience headaches, seizures, altered consciousness, and neurological focal symptoms. As a result of increased venous pressure, reduced cerebrospinal fluid absorption, and localised oedema of the brain brought on by cerebral vein thrombosis, major sinus thrombosis, and venous infarction, the intracranial pressure rises. [6] Two important trimethylation and trans-sulfuration mechanisms control the metabolism of homocysteine. Folate, vitamin B12, and vitamin B6 participate in these pathways catalytic or conversion processes. These vitamin deficiencies lead 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. [7] One or more of the brain's dural sinuses are blocked in patients with cerebral venous thrombosis, which frequently occurs in conjunction with cortical vein thrombosis [7]. Isolated cerebral vein thrombosis is the name given to a condition

in which a small percentage of individuals solely have an occluded cortical vein. Blood and cerebrospinal fluid flow are reduced as a result of cerebral venous thrombosis, and in around 50% of patients, this causes the formation of a venous infarct. Cerebral venous thrombosis, which is a leading cause of stroke in the young [7], mostly affects young adults and children in contrast to arterial infarcts. Prior to the development of antibiotics, cerebral venous thrombosis 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 thrombophillias, puerperium, neoplasms, dehydration, and pregnancy [1-3,21]. The hypercoagulability brought on by using oral contraceptives, particularly in Western nations, increases the risk of cerebral venous thrombosis [17–19]. 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 [19]. In many studies they observed the correlation of cerebral venous thrombosis and homocysteine also they found that the association of cerebral venous thrombosis and Hyper-Homocystenemiais present. Additionally, they found that total homocysteine continues to be an important risk factor for cerebral venous sinus thrombosis in subjects with confirmed thrombosis [13,14]. 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 cerebral venous thrombosis and estimate the correlation of vitamin b12 and homocysteine in subjects with cerebral venous thrombosis. In our study we have included total 55 patients after following inclusion and exclusion criteria. We have observed in our study that majority of the patients were male compared to female in the ratio of 1.11: 1. Also we have observed maximum patents were from age group of 21 – 40 years of age followed by 41 – 60 years and 61 -80 years, we had minimum patients observed in the age group of less than 20 years of age. Mean age of all the patients was 42.45 years with standard deviation of 18.25 years, among

all the patients only 8 patients with some comorbidities like HNT, DM, Epilepsy etc shown in the above table, out of that hypertension and diabetes mellitus were more common. Study conducted by Sanskriti Kamran et al [1] observed that most common age group of presentation with Cerebral venous thrombosis are 21-40 years :71.05% (21-30 years: 36.84% & 31-40 years: 34.21%) with a slight male (60.53%) prevalence in comparison to female (39.47%). In 56.58% of patients no associated comorbidity was found in the study population. Another study by Sohan B et al observed that majority were from age group of 31- 40 years (33.87 %) followed by 19-30 years (25.81%). Male patients (66.13 %) were more than females (33.87 %). Makoto Takemaru et al. 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, 8.2% of the patients were over 65 years old, and 74.5% of the patients were female, which is contrary to our study's findings regarding gender. According to studies by Shindo et al. and Ohara et al. [15] [16], the average age of cerebral venous thrombosis patients in Japan was forty-nine years old and fifty years old and female patients were 50% and 59%, respectively. This study suggests that cerebral venous thrombosis patients in Japan may be elder and have fewer females than those in Western countries, but in our study, we observed not only older patients but we had younger patents too. In our study, majority of the patients had location of thrombosis was Left Occipital and temporal regions followed by Right Frontal and Parietal, left frontal temporal parietal, left high parietal, Left Temporal, Right Frontal and Left Occipital and others. According to a study by M.A. Al Baklawy et al, 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 [1] most affected are left transverse & sigmoid sinuses (55.26%) followed by right transverse sinus & sigmoid sinuses (35.53%) Study by Makoto Takemaru et al 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 our investigation revealed that just 62.5% of people experienced headaches. Similar to our study another study by M.A.Al Baklawy et al observed that, the 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. The most typical sign of cerebral venous thrombosis is a headache. In International study on cerebral vein and dural sinus thrombosis, Patients with cerebral venous thrombosis who had no headache were mostly elderly men. Because there were so many older men in this trial, there was a low incidence of headache (62.5%). 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, in that 40% of the patients rise in homocysteine level was mild, followed by moderate rise and normal level, we have found 4(7.3) patients with Severe Hyper-homocystenemia, overall we had 81.8% of the patients had elevated levels of homocysteine, in comparison of homocysteine between male and female, it was observed that around 89.65% of the male patients rise in homocysteine was mild to severe while among female73.07% of the patients had raised homocysteine level between mild to moderate. we didn't find any of the patients among female with severe Hyper-homocystenemia, though levels of Hyper-Homocystenemia was maximum among male compared to female, 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 majority of the mean 91.60% of the patients rise in homocysteine level was in mild to moderate range and in the age group of 21 – 40 years, 82.74% of the patients had raised homocysteine level was in mild to severe range. Among all only 4 patients we have observed having severe Hyper-Homocystenemia each of 2 from age

group of 21 – 40 and 61 – 80 years of age respectively. Study by M.A.Al Baklawy et al 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 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 and 24 patients had normal levels of serum homocysteine. The mean of serum homocysteine levels was 28.58±17.74 (Normal- 24, Moderate- 16, Intermediate-36, Severe - 0). One more similar to our study by Manasi Harale et al [46] 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 cerebral venous thrombosis. Homocysteine levels should therefore be considered in the early prothrombotic workup for idiopathic venous thrombosis. Carlos Cantu et al [16] conducted study on 45 patients of cerebral venous thrombosis, concluded that high plasma concentrations of homocysteine were related with increased risk of cerebral venous thrombosis. Taheraghdam, et al. reported that patients with cerebral venous thrombosis had raised homocysteine levels. According to a study by Sohan B et al, raised levels of homocysteine is one of the risk factors in the aetiology of cerebral venous thrombosis patients. Levels of Homocysteine were shown to be considerably higher in patients with cerebral venous thrombosis. In the study by Patel J. D. et al., the mean homocysteine level was 13.88 +/- 3.86 mol/l in the control group and 33.02 +/-17.41 mol/l in the study group. It was determined to be statistically significant when they calculated the P value, and the rate of significance is higher in the study group than in the control group. It suggests that cerebral venous thrombosis and increased homocysteine levels are related. Homocysteine may play a role in oxidative damage to vascular endothelial cells, increased smooth muscle cell proliferation, and oxidative modification of low-density lipoprotein, all of which contribute to atherosclerosis and ultimately coronary artery disease, as evidenced by the higher homocysteine levels in cerebral venous thrombosis that we

observed in our study. 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. Their findings were consistent with three case-control studies [13–15] which included more than 200 well-documented individuals with idiopathic deep vein thrombosis episode. Our study observed that there was deficiency of vitamin B12 was observed among 71% of the patients, in that 45.5% of the patients had severe deficiency of vitamin B12 and in 25.5% had moderate deficiency, we have not encountered with any major difference in the Vitamin B12 levels between male and female as well as in different age groups. M.A.Al Baklawy et al conducted a study on elevation in the level of homocysteine level was due to the deficiency of vitamins like B12, also they added that Hyper-Homocystenemia is a correctable factor in cerebral venous thrombosis and can be treated with vitamin supplements, dietary adjustments, and lifestyle modifications. Hyper-Homocystenemia should be taken into consideration as a potential risk factor for cerebral venous thrombosis. Supported to our study, study by Sanskriti Sharma et al of 76 subjects of CVT, 18 subjects had mild deficiency, 07 subjects had severe deficiency, 30 subjects had normal levels and 21 patients had high level of Serum B12. The mean of Serum B12 levels was 824.9±430.8. In a similar study conducted by Manasi Harale et al (46), Patients with cerebral venous thrombosis did not have any association between their vitamin B12 levels. According to the study, Hyper-Homocystenemia may not necessarily be connected to low vitamin B12 levels, although Homocystine levels tend to be high if vitamin B12 levels are low. Carlos Cantu et al (16), concluded that low folate and vitamin B12 levels were associated with an increased risk of cerebral venous thrombosis in the population in which low socioeconomic and deficient nutritional status may contribute to its relatively high incidence. Kalita et al 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 (4).

Correcting dietary vitamin B12 deficiency may be a simple and affordable way to stop cerebral venous thrombosis caused by hyper-homocystenemia. A lack of vitamin B12 may have multiple causes. It has been stated that vitamin B12 insufficiency is frequent in north India (34). A foundation for preventing cerebral venous thrombosis in these patients may be established if the relationship between homocysteine and vitamin B12 deficiency in cerebral venous thrombosis is confirmed. Taheraghdam, et al. studied that in earlier studies, it was discovered that men were more likely than women to have raised homocysteine levels [13,14], but in our analysis, there was no obvious gender difference in the condition's prevalence. In Mexican persons, Cantu et al. discovered that raised levels of homocysteine and low vitamin B12 levels had separate associations with the incidence of CVT, indicating that not only Hyper-Homocystenemia other process also should be taken into consideration. According to J.D. Patel et al., vitamin B12 plays a significant role in the metabolism of homocysteine through the transsulfuration and remethylation pathways. Homocysteine levels in the blood rise when one of these is defective. Animal food is the main source of vitamin B12. Most Indians, especially Gujaratis, are strict vegetarians. Due to their strict vegetarian diet, they are more prone to vitamin B12 deficiencies. In this study we have found negative correlation between homocysteine and vitamin B12, but that correlation was not statistically significant (P-value = 0.055). Another study by Patel J. D. et 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 found Homocysteine levels have a negative relation with vitamin B12 levels (Pearson correlation coefficient: 0.3874; P = 0.0005). These observation supports this study; we have found highly significant association between levels of homocysteine and vitamin B12 level.

SUMMARY & CONCLUSION

❖ SUMMARY

- Majority of males suffered with cerebral venous thrombosis (CVT) compared to females.
- Majority of the patients from age groups of 20-40 years, followed by each of 21.8% from 40-60 years and 61-80 years, there were only 2 patients from age group < 20 years, both patients had age of 18 years.
- 8 patients with some comorbidities like HNT, DM, Epilepsy etc.
- Left Occipital and temporal regions, Right Frontal and Parietal, left frontal temporal parietal, left high parietal, Left Temporal were major location of thrombosis.
- Superior Sagittal Sinus, Left Sigmoid & transverse Sinus were major sinus involved.
- Maximum patients have observed the symptoms of headache, vomiting, weakness seizures and giddiness, only 2 patients observed with blurring of vision and 4 patients found with loss of speech.
- 40% of the patients raise in homocysteine level were mild, followed by moderate level and normal level, we have found 4 patients with Severe Hyper-Homocystenemia.
- Majority of patients observed with severe deficiency of vitamin B12, followed by normal. Also, we have observed 25.5% of the patients had their vitamin B12 mildly deficient.
- Mean Hb level were in normal range, only few patients had Hb level below 10 gm/dl, most of them were females.
- Except 5 patients all the patients platelets count was normal and above 1.5lakhs per microliters.
- Maximum patients had there GCS scale was more than 12.

- There was no statistically significant difference of homocysteine levels between male and females, it was comparable in both the groups. (P-value = 0.136)
- The levels of vitamin B12 in males and females did not differ statistically; they were similar in both groups. (P-value=0.345)
- There was comparable age group between the male and females (p-value = 0.302)
- Distribution of Homocysteine levels among the different age groups was not statistically significant. (P-value=0.704)
- Distribution of Vitamin B12 levels among the different age groups was not statistically significant. (p-value =0.96)
- The fraction of vitamin B12 among the various homocysteine levels differed significant statistically. The majority of vitamin B12 deficient individuals had mild to moderate homocysteine levels. (p-value<0.001) No laboratory parameters were significantly different, between raised and normal level of homocysteine.
- Correlation between Homocysteine level and other parameters like Vitamin B12, GCS score, Prothrombin Time, Platelets counts and Hb level was not statistically correlated. Only we found Homocysteine level and Vitamin B12 level was significant negatively correlated at 10% level of significance.

CONCLUSION

From overall observation and discussion with other studies we can conclude that, our results support the theory that Hyper-Homocystenemia is connected to a higher risk of cerebral venous thrombosis. Furthermore, a high risk for cerebral venous thrombosis was substantially associated with low vitamin B12 levels. Further, long-time studies with large sample size are needed to assess the mechanism and effect of Hyper-Homocystenemia, low vitamin B12, on the risk of cerebral venous thrombosis. In our study males were majorly affected, Serum homocysteine estimation in casuality of all patients of Cerebral Venous Thrombosis and periodically in yearly follow up should be recommended. This has clinical significance since supplemental therapy can be used to correct these acquired risks and stop cerebral venous thrombosis from recurrence.

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ANNEXURE I

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

IEC/NO-9/2021
Date-22/01/2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Correlation of cerebral venous sinus thrombosis with Vitamin B12 and homocysteine levels

Name of PG student: Dr G Sahith Reddy, Department of Medicine

Name of Guide/Co-investigator: Dr Mallanna Mullimani, Professor of Medicine

DR .S.V.PATIL
CHAIRMAN
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

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ANNEXURE II

SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586 103

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT: "CORRELATION OF CEREBRAL VENOUS SINUS THROMBOSIS WITH VITAMIN B12 AND HOMOCYSTEINE LEVELS"

PG GUIDE : DR. M.S. MULLIMANI

PG STUDENT : DR. G. SAHITH REDDY

PURPOSE OF RESEARCH : I have been informed about this study. I have also been given a free choice of participation in this study.

BENEFITS: -

I understand that my participation in this study will help the investigator to diagnose the disease better and will help in the management of the disease.

PROCEDURE: -

I understand that relevant history will be taken and I will undergo detailed clinical examination after which necessary investigations will be done and accordingly treatment will be given.

RISK AND DISCOMFORTS: -

I understand there is no risk involved and I will experience no pain during the procedures performed.

CONFIDENTIALITY: -

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION: -

I understand that I may ask more questions about the study at any time Concerned. The researcher is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during this study, which may influence my continued participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION: -

I understand that my participation is voluntary and I may refuse to participate or may withDRaw consent and discontinue participation in this study at any time without prejudice. I also understand that the researcher may terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician, if this is appropriate.

INJURY STATEMENT: -

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Investigator / P. G. Guide Date

I confirm that .....(Name of the PG guide / chief researcher) has explained to me the research, the study procedures that I undergo and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

_____

_____

Participant / guardian Date

_____

_____

Witness to signature Date

ANNEXURE-III: SCHEME OF CASE TAKING PROFORMA

B.L.D.E (DEEMED TO BE UNIVERSITY)

SHRI B M PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA, KARNATAKA

Informant:

Case No:

Name: IP No:

Age / Sex: DOA:

Occupation:

Address:

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

PERSONAL HISTORY:

1. Diet:
2. Appetite:
3. Sleep:
4. Bowel and bladder:
5. Habits:

FAMILY HISTORY:

MENSTRUAL HISTORY:

TREATMENT HISTORY:

GENERAL PHYSICAL EXAMINATION:

Vitals:

1. PR:
2. BP:
3. RR:
4. TEMPERATURE:
5. SpO2

Pallor:

Icterus:

Cyanosis:

Clubbing:

Lymphadenopathy:

Edema:

SYSTEMIC EXAMINATION:

1. CENTRAL NERVOUS SYSTEM:
2. RESPIRATORY SYSTEM:
3. PER ABDOMEN:
4. CARDIO VASCULAR SYSTEM:

INVESTIGATIONS:

1. Complete blood count:
2. Lipid profile:
3. Viral markers:
4. Renal function test:
5. Computed tomography:
6. Magnetic resonance imaging:
7. Prothrombin time:/ International normalized ratio:
8. Serum homocysteine:
9. Vitamin B12:

FINAL DIAGNOSIS:

TREATMENT:

Date:

ANNEXURE IV

MASTER CHART

KEY TO MASTER CHART
HB: HAEMOGLOBIN
MCV: MEAN CORPUSCULAR VOLUME
MCH: MEAN CORPUSCULAR HEMOGLOBIN
ESR: ERYTHROCTE SEDIMENTATION RATIO
PT: PROTHROMBIN TIME
INR: INTERNATIONAL NORMALIZED RATIO
GCS: GLASSGOW COMA SCALE

	A	B	C	D	E	I	J	K	L	M	N	O	S	T	U	V	W	X	Y
1	Sr. No	IP Adress	Name	Age	Sex	Symptoms	Comorbidit	Location of Thrombosis	Sinus Involvement	b Lev	MCV	MCH	elets Co	ESR	mocyste	tamin B1	PT	GCS	Outcome
2	1	338521	hanmantrai	47	m	sided weakness, seizures ,altered seron	nil	Right Frontol and Parietal	Superior Sagital Sinus	15	97	36	2.27	20	50	50	14.7/1.2	11	Improved
3	2	323818	manjula	30	f	headache	nil	Left Parietal Temporal	Left Transverse Sinus	11	85	28	5.46	15	55	150	15/1.3	15	Improved
4	3	232082	pushpa	22	f	headache	nil	Left Occipital Lobe	Left Sigmoid & transverse Sinus	12	87	30	2.53	15	25	50	11/1.0	15	Improved
5	4	232960	laxmi	20	f	left side ul, ll weakness, loss of speech	nil	Right Frontol and Parietal	Superior Sagital Sinus	9.7	76	25	3.33	10	20.6	300	13.8/1.2	10	Improved
6	5	23976	akshay	24	m	headache, vomiting	nil	Staight Sinus	Left Sigmoid & transverse Sinus	14	80	34	2.27	20	60.5	73	12.9/1/1	15	Improved
7	6	132982	shaguntala	70	f	decreased responsiveness, giddines	nil	eft parietal occipital Temporal Lobu	Left Sigmoid & transverse Sinus	10	93	30	2.18	25	26.61	59	13.1/1.1	12	Improved
8	7	121906	anil kumar	31	m	altered sumorium	nil	Left Temporal	agital Sinus, Lateral Transverse,	15	93	27	2.46	50	18.13	656	12.9/1.1	10	Improved
9	8	1323	lalithabai	71	f	seizures	htn, epileps	Left high parietal	Diffuse Venous Sinus	12	85	26	3.01	38	13.24	171	12.5/1.1	10	Improved
10	9	3556	dumdamma	65	f	bluntary movements and altered sumor	htn,dm,ihd	Right Frontol Lobe hemmhorage	Superior Sagital Sinus	12	84	27	1.98	50	11.01	200	11/1.0	10	Improved
11	10	345674	rajashekhar	31	m	rred speech with right sided weakness,	nil	Left frontal temporal parietal	eft Transverse Sinus and Sigmoi	15	96	32	2.35	60	166	30	13.2/1.1	15	Improved
12	11	4643	mohan	35	m	s of left ul and deviation of mouth to r	nil	Right Frontol and Parietal	nsverse sigmoid and internal jug	16	89	30	2.63	10	2.87	150	13.4/1.16	15	Improved
13	12	74482	hanmantraya	26	m	headache	nil	Left Occipital and temporal regions	Left Sigmoid & transverse Sinus	15	80	30	2.5	15	35.54	337	11.8/1.0	15	Improved
14	13	277127	vidya	32	f	loss of speech	nil	Right Side of Mid Brain	Internal cerebral veins	9	71	22	4.52	10	2	150	21.1/2.47	10	Improved
15	14	197309	taskeen	29	f	headache, blurring of vision	nil	Left Occipital and temporal regions	Left Sigmoid & transverse Sinus	10	80	30	2.5	12	2.87	300	9/1.1	15	Improved
16	15	280222	kamlabai	73	f	involuntary movements B/L,UL,LL	htn,dm	Anterior part superior sagital sinus	Thrombosis of veins of trocand	13	91	29	1.82	25	8.83	94	12.4/1.0	15	Improved
17	16	93417	sujatha	26	f	headache	nil	Left Occipital and temporal regions	Left Sagital transverse vein	14	75	30	2.5	10	5	217	17/1.6	15	Improved
18	17	108948	shoba	21	f	generalised weakness, vomiting	nil	Left Frontal parieto temporal	rior Sagital and right transverse	9.1	72	21	1.5	10	40	100	13.6/1.0	15	Improved
19	18	105799	yamanappa	38	m	slurring of speech,giddiness	nil	Left Frontal parieto and Capsulo	Left Sigmoid & transverse Sinus	17	93	29	1.84	15	3.9	200	14.4/1.25	15	Improved
20	19	186588	basavaraj	45	m	vomiting, giddiness	nil	Cerebral Hemisphere and cerebral	Internal cerebral veins	14	87	30	2.22	10	30	20	11/1.0	15	Improved
21	20	181817	dharmaji	60	m	headache,vomiting	nil	Bellow Frontol Parietal region	Superior Sagital Sinus	15	89	33	4.45	5	65	184	12.6/1.0	15	Improved
22	21	6165	hemamalini	18	f	headache, seizures	nil	Left Occipital and temporal regions	eft Transverse Sinus and Sigmoi	10	99	30	2.63	10	35	20	11/1.0	15	Improved
23	22	160792	anil	51	m	headache	nil	left temporal	Superior Sagital Sinus	13	99	27	120	30	2	900	11/1.0	15	Improved
24	23	299302	meenakshi	21	f	headache	nil	Left Temporal	eft transverse and internal jugle	9.1	99	26	3.15	20	21	257	12/1.2	15	Improved
25	24	12633	shilpa	26	f	headache	nil	Left Occipital and temporal regions	eft transverse and internal jugle	10	99	30	1.5	30	60	30	11/1.0	15	Improved
26	25	151792	chandrakeshar	30	m	giddiness, fever,headache	nil	Left high parietal	Diffuse Venous Sinus	16	99	32	1.36	50	35	20	11/1.0	15	Improved
27	26	190660	sidhaling	24	m	giddiness	nil	Right Frontol	Superior Sagital Sinus	12	99	26	2.33	20	609	20	12.9/1.1	15	Improved
28	27	362782	shri krishna	23	m	seizures	nil	Left high parietal	Diffuse Venous Sinus	9.1	99	18	3.01	40	13.24	171	12.5/1.5	10	Improved
29	28	251528	sangeeta	28	f	headache	nil	Right Frontol	Superior Sagital Sinus	15	99	27	6.1	10	10	120	17.2/1.5	15	Improved
30	29	93417	sujatha	26	f	headache, seizures	nil	Left Temporal	uperior Sagital lateral transvers	16	99	21	3.01	30	2.05	217	12.5/1.1	15	Improved
31	30	172604	hussanabai	55	f	vomiting	nil	Left frontal temporal parietal	erior Sagital & Left transverse S	16	99	21	8	50	43.8	20	13.2/1.1	10	Improved
32	31	374100	vimalabai	45	f	giddiness,numbness	nil	Below Frontol parietal	eft transverse and internal jugle	14	99	30	3.67	30	3.59	421	12/1.0	15	Improved
33	32	362782	shri krishna	30	m	giddiness,fall	nil	Thalmic Blood	Left Transverse Sinus	16	99	33	3.36	30	35.98	78	11/1.0	15	Improved
34	33	379474	salam mulla	22	m	vomiting,fever,irregular movemnts	pilepsy,poli	Left anterior frontal Lobe	rior Sagital and right transverse	12	99	27	1.67	10	3.36	34	11/1.0	15	Improved
35	34	20712	hushen	70	m	left sided weakness, seizures	nil	Right Frontol and Parietal	Superior Sagital Sinus	13	99	34	2.27	13	50	50	14.7/1.2	11	Improved
36	35	19807	dunawwa	80	f	headache	nil	Left Parietal Temporal	Left Transverse Sinus	10	99	28	5.46	20	55	150	15/1.3	15	Improved
37	36	24229	laxmibai	21	f	headache	nil	Left Occipital	Left Sigmoid & transverse Sinus	12	99	30	2.53	15	25	50	11/1.0	15	Improved
38	37	142084	annappa	30	m	left side ul, ll weakness, loss of speech	nil	Right Frontol and Parietal	Superior Sagital Sinus	9.7	99	25	3033	20	30	300	13.8/1.2	10	Improved
39	38	135367	hanarashekha	31	m	headache,vomiting	dm	Left Parietal	Left Transverse Sinus	11	99	28	5.46	15	55	150	15/1.3	15	Improved
40	39	127367	shivalingaya	40	m	fever,seizures	nil	Left frontal temporal parietal	t sinus, left transverse, sigmoid	15	99	34	2.27	20	60.5	75	12.9/1.1	15	Improved
41	40	26124	sharanappa	26	m	s of left ul and deviation of mouth to r	nil	Right Frontol and Parietal	eft transverse and internal jugle	16	99	28	2.63	10	2.87	150	13.4/1.16	15	Improved
42	41	156102	dmakshyami	68	f	altered sumorium	nil	Left Temporal	rior Sagital Sinus, tranverse & sig	15	99	27	2.46	50	18.13	656	12.1/1.1	10	Improved
43	42	65537	srimanth	70	m	seizures	htn, epileps	Left high parietal	Diffuse Venous Sinus	12	99	26	3.01	38	13.24	171	12.5/1.1	10	Improved
44	43	22481	basamma	40	f	bluntary movements and altered sumor	htn,dm	Right Frontol Lobe hemmhorage	Superior Sagital Sinus	12	99	27	1.78	50	11.01	200	11/1.0	10	Improved
45	44	13049	shivayogi	70	m	rred speech with right sided weakness,	nil	Left frontal temporal parietal	Left Sagital transverse vein	15	99	32	2.35	60	166	30	13.2/1.1	15	Improved
46	45	25337	ramu	50	m	s of left ul and deviation of mouth to r	nil	Left frontal parietal	eft transverse and internal jugle	16	99	30	2.63	10	2.87	150	13.4/1.16	15	Improved
47	46	133042	shrutappa	70	m	headache , blurring of vision	nil	Left Occipital and temporal regions	Left Sigmoid & transverse Sinus	11	99	28	2.5	12	2.87	300	9/1.1	15	Improved
48	47	251478	sharanappa	60	m	loss of speech	nil	Right Side of Mid Brain	Internal cerebral veins	9	99	22	4.52	10	2	150	33.1/2.94	10	Improved
49	48	78318	sarabai	68	f	headache	nil	Left Occipital and temporal regions	Superior Sagital Sinus	15	99	30	2.5	15	35	300	11.8/1.0	15	Improved
50	49	94283	ganjaram	40	m	vomiting, giddiness	nil	Cerebral Hemisphere and cerebral	Internal cerebral veins	14	99	30	2.22	10	30	20	11/1.0	15	Improved
51	50	130519	manjula	45	f	generalised weakness, vomiting	nil	Left frontal temporal parietal	rior Sagital and right transverse	9.1	99	21	1.5	10	40	100	13.6/1.0	15	Improved
52	51	277127	vidya	32	f	giddiness	nil	Right Frontol	Superior Sagital Sinus	13	99	37	2	20	60	20	12.9/1.1	15	Improved
53	52	306953	mamta	45	f	headache	nil	Left high parietal	Diffuse Venous Sinus	13	99	26	3.01	40	13.22	170	12.5/1.1	15	Improved
54	53	101728	ashok	55	m	fever, vomiting	nil	Left anterior frontal Lobe	Superior Sagital Sigmoid Sinus	12	99	27	1.67	20	50	50	14.7/1.2	15	Improved
55	54	94283	gangaram	68	m	left sided weakness, seizures	htn	Left frontal parietal	Superior Sagital Sinus	13	99	34	2.27	13	200	50	12.5/1.1	13	Improved
56	55	94865	bapu	56	m	headache	nil	Left Occipital	Left Sigmoid & transverse Sinus	12	99	30	2.53	15	25	50	11/1.0	15	Improved