STUDY OF HYPERHOMOCYTEINAEMIA AS A RISK FACTOR FOR ATEROTHROMBOTIC CEREBROVASCULAR ACCIDENT IN YOUNG ADULTS

HOW TO CITE THIS ARTICLE:

ABSTRACT: AIMS: The present study was undertaken to assess the prevalence of hyperhomocysteinemia in young adults with atherothrombotic CVA and to find the association between levels of homocysteine and atherothrombotic CVA. METHODOLOGY: This observational study was conducted in the Department of Medicine, Dr. D. Y. Patil Medical College Hospital and Medical Research Centre, Kolhapur, Maharashtra on 30 young patients with ischaemic stroke proved by CT/MRI/MS venogram. Plasma homocysteine was estimated by the Axis Homocysteine Enzyme immunoassay. RESULTS: Of the 30 patients, 73% were males and 27% were females with male to female ratio of 2.7: 1.50% were aged between 41 to 50 years. Overall the mean age was 39.27±7.67 years. Overall mean plasma homocysteine levels were raised (23.70±11.67µmol/L). CONCLUSION: Plasma homocysteine levels were raised in 56.67%. Hyperhomocysteinemia was significantly associated with age whereas sex, blood pressure, raised blood sugar levels, low haemoglobin levels and diagnosis did not influence hyperhomoceistinaemia.

KEYWORDS: Homocysteine; Hyperhomocysteinemia; Ischaemic stroke; Stroke in young.

INTRODUCTION: Stroke in young poses a major health problem. WHO defines stroke as an event caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue. The most common symptom of a stroke is sudden weakness or numbness of the face, arm, or leg, most often on one side of the body, occurring in 90% of the strokes. Other symptoms include confusion; difficulty speaking or understanding speech; difficulty seeing with one or both eyes; difficulty walking, dizziness, and loss of balance or coordination; severe headache with no known cause; fainting or unconsciousness. The effects of a stroke depend on which part of the brain is injured and how severely it is affected. A very severe stroke can cause sudden death. This happening in the younger age group adds to the social burden, and as such these patients merit special attention in diagnostic, therapeutic, and preventive care. It leaves the patients with residual disabilities like physical dependence, cognitive decline, depression, and seizures.

Hyperhomocysteinemia, defined as an elevated plasma total homocysteine concentration (>10µM), is one such factor. Some studies have shown that elevated serum homocysteine is an independent risk factor for stroke. However, studies on the role of homocysteine among young patients with stroke are scarce and so far few studies have elaborated the role homocysteine in Indian context. Hence the present study was undertaken to assess the prevalence of hyperhomocysteinemia in young adults with atherothrombotic CVA and to find the association between levels of homocystein and atherothrombotic CVA.
METHODOLOGY: The present one year observational study was conducted at the Dr. D. Y. Patil Medical College Hospital and Medical Research Centre, Kolhapur, Maharashtra on patients with ischaemic stroke. A total of 30 patients with ischaemic stroke (Proved by CT/MRI/MR venogram and aged between 18 to 45 years) admitted in the wards of Medicine Department, were studied. Patients on haemodialysis/renal transplants, liver disease, systemic lupus erythematosus, diabetes mellitus, hypertension, chemotherapy, oral contraceptives, coagulation disorder, connective tissue disorders, pregnant women, recent child birth, smokers, valvular heart disease, dislipidemia and on drugs such as methotrexate, theophyline, metformin, niacin, steroids were excluded from the study.

Prior to the commencement, the study was approved by the Ethical and Research Committee of the institute. All the patients (Caregivers in case of comatosed patients) were explained about the nature of study and a written informed consent was obtained before enrollment. Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded. Further these patients underwent general and specific neurologic examinations, including a thorough history. Plasma homocysteine was estimated by the Axis Homocysteine Enzyme immunoassay. The normal values of plasma homocysteine were considered as 5.90 to 16.00umol/L (Males) and 3.36 to 20.44 umol/L (Females).

The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test. The continuous data was expressed as mean ± standard deviation (SD). A probability value (‘p’ value) of less than or equal to 0.05 was considered as statistically significant.

RESULTS: Of the 30 patients studied, 73% were males and 27% were females with male to female ratio of 2.7: 1. Almost half (50%) were aged between 41 to 45 years followed by 30% between 31 to 40 years. However 20% of patients were aged between 18 to 30 years. Overall the mean age was 38.53±6.92 years.

The mean pulse rate was 77.87±8.96 bpm. The mean systolic blood pressure levels were 141.40±24.80 mm Hg and mean diastolic blood pressure levels were 83.53±8.59mm Hg.

Haemoglobin levels were normal (>12.5g%) in 56.67% patients whereas in 43.33% in haemoglobin levels were low (<12.gm%) suggestive of anaemia. Random blood sugar levels were normal (<140mg/dL) in 70% patients whereas among 30% of patients random blood sugar levels were raised (>140mg/dL). Overall mean haemoglobin (12.84±2.53gm%), WBC (9496.67 ±3278.51/mm³), platelets (242266.67±70005.88/mm³), urea (29.04±9.97mg/dL), serum creatinine (0.98±0.16mg/dL) revealed normal findings. The overall random blood sugar levels were raised (159.42±101.60mg/dL).
Plasma homocysteine levels were normal in 43.33% patients whereas in 56.67% raised. Overall mean plasma homocysteine levels were raised (23.70±11.67umol/L).

The commonest diagnosis was left hemiparesis (40%) followed by right hemiparesis (26.67%). Central venous sinus thrombosis was noted in 23.33% of patients. In the remaining 3.33% each had cerebellar infarct, thalamic capsular infarct and transient ischaemic attack.

Of the 30 patients 22 were males and 8 were females. Among them 54.55% males and 62.50% females had raised plasma homocysteine. However this difference was statistically not significant (p=0.697).
Of the 15 patients aged between 41 to 45 years 80% had raised plasma homocysteine levels suggesting statistically significant association of age with hyperhomocysteinemia (p=0.020).
No statistically significant difference was noted between hyperhomocystinemia and blood pressure (p=0.087), haemoglobin levels (p=0.310) and random blood sugar levels and raised plasma homocysteine levels (p=0.936). Of the 12 patients who had left hemiparesis. Of these 6(50%) each had raised plasma homocysteine. The distribution of other patients with raised and normal plasma homocysteine levels is as shown in table 27. However plasma homocysteine levels did not influence the diagnosis (p=0.674). Similarly the qualitative assessment of these variables showed no statistically significant association (p>0.05).

**DISCUSSION:** In the present study plasma homocysteine levels were normal in 43.33% patients whereas in 56.67% raised plasma homocysteine levels were noted. Overall mean plasma homocysteine levels were raised (23.70±11.67umol/L). Many studies have showed that increased homocysteine represents an independent risk factor for coronary, cerebrovascular and peripheral arterial disease. A similar study by Kristensen et al in a case control study of 80 consecutive patients aged 18-44 years with first ever ischemic stroke and 41 healthy control subjects showed that moderate increase in homocysteine levels after methionine loading was associated with an increased risk for ischemic stroke in young adults.

Another study by Kalita A et al, to compare the risk factors, nature of stroke and outcome of patients with and without hyperhomocysteinemia reported that serum homocysteine was elevated in 60.6% of patients. Though the number of patients with hyperhomocysteinemia reported were comparable to the present study, it could not compared as the authors in previous study assessed the serum homocysteine and in general population whereas present study focused plasma homocysteine levels in young adults.

Boysen et al in a longitudinal study of 1039 stroke patients (mean age, 75) measured homocysteine levels after primary admission. These patients were followed up for 15 months. Serum homocysteine was significantly higher in 105 patients who experienced a recurrent stroke during the follow up period than in patients without recurrence. At the index event, serum homocysteine was significantly higher in 909 patients with ischemic cerebrovascular events than in 130 patients with intracerebral hemorrhage.

Various risk factors for cerebrovascular accidents like age, sex, food habit, hypertension, diabetes mellitus, life style were studied and analyzed in relation to serum homocysteine levels. Hyperhomocysteinemia is one of the newly recognized factor that increase the risk of vascular disease. Mechanisms by which hyperhomocysteinemia increases risk of cerebrovascular accidents are not clear, but several possible mechanisms have been proposed.

Hyperhomocysteinemia is associated with premature atherosclerosis. Experimental studies both in vivo and in vitro shows that homocysteine causes endothelial injury and cell detachment. Hence these data suggest that homocysteine might contribute to cerebrovascular disease in patients as an additive risk factor. Further the mechanisms by which hyperhomocysteinemia increases risk of stroke in young are not completely understood. It is postulated that, Artery-to-artery embolism and dissection may cause stroke in young adults with homocystinuria. The results also support a rationale for screening for hyperhomocysteinemia in young adults with stroke without a phenotype suggestive of classic homocystinuria.

In this study of the 15 patients aged between 41 to 50 years 80% had raised plasma homocysteine levels suggesting statistically significant association of age with hyperhomocysteinemia (p=0.020). The mean plasma homocysteine levels were high (27.50±19.86umol/L) in
patients aged between 18 to 30 years compared to those aged between 31 to 40 years (16.02±5.91umol/L) and 41 to 45 years (26.79±8.18umol/L; p=0.056). According to findings of Longo et al,11 increase in the serum homocysteine levels were observed with increasing age.

The strength of the study was we meticulously analysed the data both qualitatively and quantitatively. However, due to smaller sample size the findings of the present study needs further evaluation on large population which would further enlighten the precise role of homocysteine in young patients with stroke.

CONCLUSION: The present showed hyper-homocysteinaemia in 56.67% patients. No association of sex, blood pressure, raised blood sugar levels, low haemoglobin levels and diagnosis with hyperhomoceistinaemia (p>0.050) whereas age was significantly associated with hyperhomoceistaemia.

BIBLIOGRAPHY:
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None

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