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SERUM HOMOCYSTEINE LEVEL AMONG YOUNG PATIENTS WITH CEREBROVASCULAR ACCIDENT

Neurology

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ABSTRACT

Background: Stroke is defined as a focal (or at times global) neurological impairment of sudden onset. In general, stroke in young includes subjects falling under the age group of 15-45 years. It is more heterogeneous due to wide variety of possible underlying risk factors and etiologies. Hyperhomocysteinemia leads to proliferation of vascular smooth muscles, which oxidatively damages the vascular endothelium and creates a prothrombotic environment thus promoting carotid atherosclerosis, lacunar infarction, and increased risk of stroke. **Methods:** It is a hospital based observational study including patients attending OPD/IPD at Departments of Medicine and Neurology, Assam Medical College and Hospital, Dibrugarh, Assam over a period of one year (1st July 2021 to 30th June 2022). 90 first ever stroke patients aged 15-45 years were included. Serum sample was stored and homocysteine estimated by ELISA. Statistical differences was measured between various stroke groups using student t- test and a p value of <0.05 was considered statistically significant. **Results:** Mean age for all the cases was 39.43 ± 5.71 years. Male preponderance was seen (55.55%). Majority of the stroke cases were haemorrhagic (56.66 %). The average serum homocysteine was higher in ischemic stroke (35.14±10.85 µmol/L) than in haemorrhagic stroke (23.28±7.58 µmol/L) (p-value of 0.0279) **Conclusions:** Routine inclusion of serum homocysteine level estimation in young patients with stroke is strongly suggested to assess the risk of stroke as well as measures should be taken whenever necessary to reduce the homocysteine level to prevent various cerebrovascular complications.

KEYWORDS

Young stroke, haemorrhage, ischemic, homocysteine.

1. INTRODUCTION

A stroke or cerebrovascular accident (CVA) is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause.[1] A focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 h (or leading to death) and of presumed vascular origin, excludes transient ischemic attack (TIA) and haemorrhage and symptoms caused by trauma.[2] Stroke in young age is an increasing problem in both developing and developed countries because of rising incidence, high morbidity and mortality and long term psychological, physical and social consequences. It is more heterogeneous due to wide variety of possible underlying risk factors and etiologies. Although various studies on stroke in young included subjects from second to fourth or fifth decade, in general, stroke in young includes subjects falling under the age group of 15-45 years.[3]

Young people globally experience roughly 23% of haemorrhagic strokes and 11% of ischemic strokes each year. The prevalence rates in the same age group are 33% for haemorrhagic strokes and 19% for ischemic strokes.[4] In India, incidence of stroke ranges from 108 to 172/100,000 persons per year, and the crude prevalence of stroke ranges from 26 to 757/100,000 persons in different parts of the country during the past decade.[5] 24-35% of all the neurological admissions in India are stroke in young.[6]

The normal level of serum homocysteine ranges between 5 to 15 µmol/L. Each increase in plasma homocysteine levels by 2.5 µmol/l leads to an increased risk of stroke by about 20%.[7] Both acquired and genetic factors can have an impact on plasma homocysteine. Male gender, aging, smoking, impaired renal function, and some drugs like corticosteroids and cyclosporine can also cause hyperhomocysteinemia. Genetic causes include classic homocystinuria and C677T homozygote mutation of 5,10-methylenetetrahydrofolate reductase (MTHFR).

Raised levels of total serum homocysteine are responsible for impairment of endothelial function and intensification of thrombosis. Animal and human studies have reported a significant association between elevated serum homocysteine and carotid atherosclerosis, lacunar infarction, and increased risk of stroke in atrial fibrillation.[8] The present study was undertaken with an aim to assess serum homocysteine levels as an individual risk factor of stroke in young patients attending Assam Medical College and Hospital, Dibrugarh.

2. METHODOLOGY

Aims and objectives

The study was undertaken with the following aims and objectives:

1. To estimate serum homocysteine level in young patients with cerebrovascular accident who were attending outpatient Departments of Medicine and Neurology or admitted in the inpatient Departments of Medicine and Neurology in Assam Medical College and Hospital, Dibrugarh, Assam.
2. To compare serum homocysteine level in different types of stroke.

Inclusion criteria

Stroke patients of 15 to 45 years of age, with only first ever stroke were included in the study.

Exclusion criteria

Patients having age less than 15 years or more than 45 years, with previous history of stroke or head trauma were excluded from the study.

Patients with renal dysfunction, connective tissue disorders, malignancies, vitamin deficiencies like folate, vitamin B_6, vitamin B_{12}, or those on certain medication use like methotrexate, antiepileptics, thaizides, etc. were also excluded from the study.

Place Of Study:
Assam Medical College and Hospital, Dibrugarh, Assam.

***Study Design*:** Hospital based observational study.

***Study Population*:**
Both male and female young cerebrovascular accident patients attending outpatient or admitted in Departments of Medicine and Neurology, Assam Medical College and Hospital, Dibrugarh were included.

***Duration Of Study*:** One year (1st July 2021 to 30th June 2022).

***Sample Size*:**
The sample size for our study was calculated to be 84, which was rounded off to be 90.

***Method Of Collection Of Data*:**

All patients who fulfilled the inclusion and exclusion criteria were included in this study. A proforma was prepared which included detailed history, clinical examination and requisite investigations available in our hospital. History included all symptoms pertaining to stroke in detail with emphasis on all the risk factors attributable to the stroke in young.

A detailed general physical examination was carried out such as BMI, nutritional status, pallor, icterus, cyanosis, pedal edema (pitting and nonpitting), jugular venous pressure. The pulse was examined for rate, rhythm, character, volume, condition of the arterial wall, radio-radial delay, and radio-femoral delay. All the peripheral arterial pulses were also examined. Blood pressure was measured, at least after 5 minutes of rest, using a standard mercury manometer and appropriate cuff, in sitting position, in the right arm, and the value was recorded. Systemic examination was done as per prespecified proforma and neurological deficits identified.

Relevant investigations like hemoglobin, total white cell count, erythrocyte sedimentation rate, routine urine analysis, blood glucose, serum homocysteine, renal function test, liver function test, serum levels of folate, vitamin B6, vitamin B12, fasting lipid profile, Chest X-ray, Ultrasonography of whole abdomen, CT scan head were done for all patients, bleeding time, clotting time, electrocardiography and echocardiogram, MRI, ANA profile, CPK, CT Thorax and Abdomen, P-ANCA and C- ANCA done for the required patients.

Statistical Analysis

Descriptive statistical analysis has been carried out in the present study. Quantitative data were expressed as mean ± standard deviation (S.D). Qualitative data were expressed as number and percentage. Qualitative data in terms of mean, median and standard deviation was calculated. Significance was assessed at 5% level of significance ($p < 0.05$). All relevant data was collected, sorted, categorised and analyzed with standard statistical tools using SPSS (Statistical Package for the Social Sciences) software (Version 20, SPSS Inc., Chicago, IL, USA).

PRINCIPLE of estimating serum homocysteine:

ELISA (Enzyme Linked Immunosorbent Assay). The fundamental principle is that the target analyte (the antigen) is recognised with high specificity by antibodies, which are proteins produced by the immune system. The immune system produces antibodies in response to the presence of antigens. These antibodies can recognise and bind to the antigens, the labelling of the bound antibody forms the basis of the detection. The colour change is detected by spectrophotometry in an ELISA reader. The intensity of the colour is directly proportional to the amount of the detection molecule (antigen or antibody) present in serum.

3. RESULTS

Table 1: Age Wise Distrbution Of Young Stroke Patients

AGE GROUPS (YRS)	NUMBER OF STROKE CASES (N= 90)	PERCENTAGE (%)
15-20	0	0
21-25	4	4.44
26-30	5	5.55
31-35	10	11.11
36-40	28	31.11
41-45	43	47.77

Table 2: Gender Wise Distrbution Of Young Stroke Patients

GENDER	NUMBER (N= 90)	PERCENTAGE (%)
Male	50	55.55
Female	40	44.44

Table 3: Type Of Stroke Distribution

TYPE OF STROKE	NUMBER (N= 90)	PERCENTAGE (%)
Ischemic	39	43.33
Haemorrhagic	51	56.66

Table 4: Stroke Patients With Homocysteine Level

SERUM HOMOCYSTEINE LEVEL	NUMBER (N= 90)	PERCENTAGE (%)
Normal	60	66.67
Elevated	30	33.33

Table 5: Age Wise Distribtion Of Hyperhomocysteinemia

AGE GROUPS (YRS)	NUMBER OF HYPERHOMOCYSTEINEMIA CASES (N= 30)	PERCENTAGE (%)
15-20	0	0
21-25	0	0
26-30	1	3.33
31-35	4	13.33
36-40	11	36.67
41-45	14	46.67

Table 6: Gender Wise Distribtion Of Hyperhomocysteinemia

GENDER	NUMBER (N= 30)	PERCENTAGE (%)
Male	16	53.33
Female	14	46.67

Table 7: Average Serum Homocysteine Level Between The Two Groups

GROUPS	AVERAGE SERUM HOMOCYSTEINE (MMOL/L) ± SD	P-VALUE
Elevated group	33.16±11.20	<0.0001
Normal group	8.65±3.06	

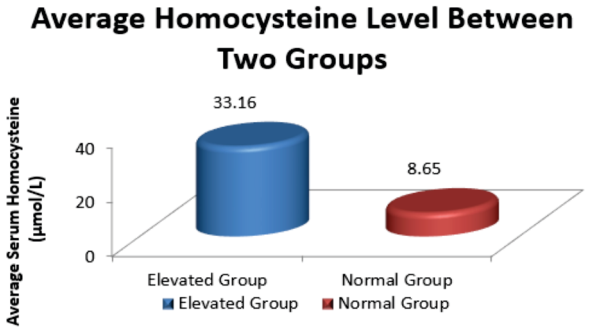
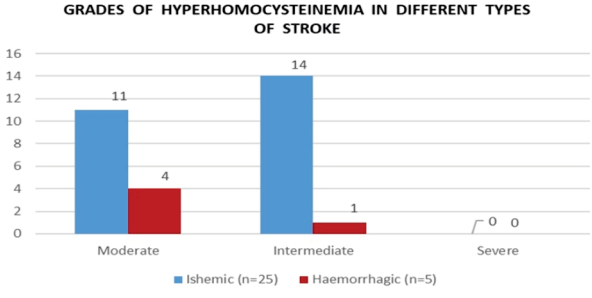


Table 8: Hyperhomocysteinemia In Different Strokes

GROUPS	AVERAGE SERUM HOMOCYSTEINE (MMOL/L) ± SD	P-VALUE
Ischemic	35.14±10.85	0.0279
Haemorrhagic	23.28±7.58	

Table 9: Grades Of Hyperhomocysteinemia In Different Types Of Stroke

GRADES OF HYPERHOMOCYSTEINEMIA	ISCHEMIC (N= 25)	HAEMORRHAGIC (N= 5)
Moderate	11 (44%)	4 (80%)
Intermediate	14 (56%)	1 (20%)
Severe	0 (0%)	0 (0%)



4. DISCUSSION

The mean age for all the cases was 39.43 ± 5.71 years. The majority of subjects belonged to the 41–45 years age group (47.77%). Hussain M *et al.*[9], Nayak SD *et al.*[10], Niazi F *et al.*[11] also found similar results with amean age of 34, 34.7 and 35.8 years respectively.

Male preponderance was seen in our study (55.55%), as was also found in studies by Lipska K *et al.*[12], Bogousslavsky J *et al.*[13]

Majority (56.66 %) of the stroke cases were haemorrhagic while 43.33% were ischemic, as also estimated by The Northern Manhattan Stroke Study[14] where 45% had ischemic stroke while 55% had haemorrhagic stroke. Singhal AB *et al.*[15] showed that 50% were ischemic while rest 50% were haemorrhagic.

Two thirds of the patients (66.67%) had serum homocysteine levels within normal range, while only one third (33.33%) had elevated levels. Similar results were shown by Yide Y *et al*.[16] and Levent G. *et al*.[17] where 35.4% and 37.9% patients respectively had elevated homocysteine levels.

Out of the 30 young patients of stroke having hyperhomocysteinemia, maximum number of patients (53.33%) were male and belonged to the 41-45 years of age group (46.67%). Yide Y *et al*.[16] in their case control study including 4012 participants having hyperhomocysteinemia, estimated that 52.5% were males while 47.5% were females and also reported a one-year increase in age to be significantly associated with 2% higher risk of hyperhomocysteinemia.

Average serum homocysteine was seen to be higher in stroke patients with hyperhomocysteinemia (33.16±11.20 µmol/L) than in stroke patients with normal homocysteine levels (8.65±3.06 µmol/L) (p-value of <0.0001). Similar findings were reported by Harris S *et al*.[18]

The average serum homocysteine was seen to be higher in ischemic stroke (35.14±10.85 µmol/L) than in haemorrhagic stroke (23.28±7.58 µmol/L) (p-value of 0.0279), similar to studies by Bokhari FA *et al*.[19] and Fang X *et al*.[20]

Most of the patients with ischemic stroke had intermediate levels of hyperhomocysteinemia (56%), while those with haemorrhagic stroke had moderate levels of hyperhomocysteinemia (80%). The finding of our study is different from other studies by Peng H *et al*.[21] and Perini F *et al*.[22] possibly because of differences in ethnicity, gender and racial distributions.

Hypertension (38.9%) was the most common risk factor associated with stroke followed by type 2 diabetes mellitus (26.67%). Smoking was associated with 24.4% of the patients. This was also supported by Nedeltchev K *et al*.[23] and Niazi F *et al*.[11]

5. Limitations Of The Study

There were certain limitations in the present study such as small study population, shorter duration of the study and missing out on some of the eligible cases because of limited human resources and time constraints. Further large scale studies are required to validate our study.

6. CONCLUSION

Stroke in young age is a matter of serious concern because of its rising incidence, high morbidity and mortality and long term psychological, physical and social consequences, both on the individual as well as the family.

In this hospital based observational study done in the North Eastern population of India, we found that there was a significant relation of the levels of serum homocysteine with different types of stroke in young. Serum homocysteine was found to be higher in ischemic than haemorrhagic stroke. Serum homocysteine level shows increasing trend with aging; it was also observed in our study.

As estimating serum homocysteine level is feasible, routine inclusion of serum homocysteine level estimation is strongly suggested to assess the risk of stroke as well as non-pharmacological and pharmacological measures should be taken whenever necessary to reduce the serum homocysteine level to prevent various cerebrovascular complications.

7. Conflicts Of Interest: NIL

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