

Evaluation of Serum Homocysteine Levels in Cerebrovascular Accidents: A Teaching Hospital Based Study

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ABSTRACT

Background: Cerebrovascular accident is an important cause of premature mortality and disability in developing countries like India. In the USA stroke is the third most common cause of mortality and morbidity after cardio-vascular disease and cancer.

Materials and Methods: Forty-six patients presenting with cerebrovascular accidents consisting of both hemorrhagic and infarction admitted in the Medicine Ward at Narayan Medical College and Hospital, Jamuhar over a period of one year and four months were enrolled in the study.

Results: We observed that blood sugar levels are higher in cases (117.24±44.21 mg/dl) than control (85.54±16.37 mg/dl) which is significant. HDL cholesterol level is significantly low in study group when compared with control group. Total cholesterol level is significantly higher in patients (187.4±44.02 mg/dl) than in controls (142.34±27.02 mg/dl) whereas no significant difference could be observed in serum triglycerides and creatinine levels. The mean homocysteine level is also higher in males than in females showing 14.94 ± 5.12 mmol/L and 13.52 ± 4.31 mmol/L respectively.

Conclusion: Serum homocysteine level as an important tool to investigate all cases of cerebrovascular accidents and also in those who are at risk of developing stroke.


Keywords: Cerebrovascular Accident, Hemorrhage, Serum Homocysteinemia.

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INTRODUCTION

Cerebrovascular accident is an important cause of premature mortality and disability in developing countries like India.¹ In the USA stroke is the third most common cause of mortality and morbidity after cardio-vascular disease and cancer.² Intracranial atherosclerosis of large vessels is most common cause of cerebro-vascular accident in India.³

Homocysteine is sulfur containing amino acid and an intermediate in methionine metabolism. Homocysteine when produced in excess is excreted out of the tightly regulated cell environment into the blood. In many individuals with inborn errors of homocysteine metabolism, kidney or liver disease, nutrient deficiencies, or concomitant ingestion of certain pharmaceuticals, homocysteine levels can rise beyond normal levels and can lead to adverse health outcomes.⁴

Stroke has occurred if the neurologic manifestations last for >24 hours or brain infarction is demonstrated on imaging study.⁵ Extensive experimental evidence, both in vitro and in vivo, indicates that homocysteine causes endothelial dysfunction. Homocysteine changes vascular tone by regulating endothelium-

dependent vasodilator and constrictor substances, including decreasing nitric oxide bioavailability, increasing contractile prostanoids as well as interfering myoendothelial communication.⁶ For healthy middle aged adult individuals, hyperhomocysteinemia is an independent risk factor for endothelial dysfunction.⁷ Elevated homocysteine level is common, and this is the major prothrombotic factor associated with stroke. Our aim was to evaluate the serum homocysteine levels in cerebrovascular accident as a risk factor for stroke.

MATERIALS AND METHODS

Study Location: Department of Medicine, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar.

Study Design: Case-control study

Ethics Approval: Study was approved by the Institutional ethics committee and informed consent was taken from the participants or from the blood relatives.

Study Period: January 2018 to April 2019.

Sample Size: Total seventy-five were recruited for this study.

Inclusion Criteria: Forty-six patients presenting with cerebrovascular accidents consisting of both hemorrhagic and infarction admitted in the Medicine Ward at Narayan Medical College and Hospital, Jamuhar over a period of one year and four months were enrolled in the study. A detailed medical history was obtained, and all patients were subjected to standard investigations including neurological examinations, brain CT scan and all routine investigations like routine blood examinations liver function test, kidney function tests, urine examination, chest X-ray, ECG, EEG etc. Other related examinations were performed when indicated. Evaluation of previous cerebrovascular events and events that occurred during the study was performed according to the World Health Organization definitions of stroke. Twenty-nine age and sex matched subjects who do not have a history or signs of cerebrovascular diseases were recruited to form the control group. Brain imaging was not performed in the controls. All patients and controls were received by one physician and were subjected to a standardized clinical assessment. For control group, individuals who are smokers, alcoholics, diabetics and hypertensive or with renal diseases were excluded from the study as such conditions are reported to have increased serum homocysteine levels.

Sample Collection: 10ml fasting blood sample of 46 cases and 29 control patients collected on admission.

Methodology: Out of another 10 ml of fasting sample collected, 2 ml was placed in fluoride vials for estimation of random blood sugar and rest of the sample was collected in polypropylene tubes to obtain serum for estimation of serum triglyceride (TG), total cholesterol, high density lipoprotein (HDL) and serum creatinine

concentrations. Estimation of serum homocysteine level by Chemiluminescent Immunofluorescent Assay by Instrument Minividas. The AMS enzymatic test for the quantitative homocysteine determination based on a series of enzymatic reaction causing a decrease in absorbance value due to NADH oxidation to NAD⁺. Homo-cysteine concentration in sample is directly propositional to the quantity of NADH converted to NAD⁺.

Statistical Analysis: Statistical analysis was done using IBM, SPSS Statistics-22 software.

RESULTS

In one year and four months of study, it was observed that incidence of CVA was more in the male population, with a male: female ratio being 2:1. Cerebrovascular accident patients and controls were well matched for age and gender Table-1. The mean homocysteine level is also higher in males than in females showing 14.94 ± 5.12 mmol/L and 13.52 ± 4.31 mmol/L respectively as seen in Fig-1.

When the levels of total homocysteine is compared between the cases and control, the study group has 14.98±5.06 mmol/L whereas in the control, it is 11.6±4.26 mmol/L which is statistically significant Table- 2. We observed that blood sugar levels are higher in cases (117.24±44.21 mg/dl) than control (85.54±16.37 mg/dl) which is significant. HDL cholesterol level is significantly low in study group when compared with control group. Total cholesterol level is significantly higher in patients (187.4±44.02 mg/dl) than in controls (142.34±27.02 mg/dl) whereas no significant difference could be observed in serum triglycerides and creatinine levels.

Table 1: Sex wise distribution mean age in cases and controls:

Gender	Study Group		P value
	Cases (Mean ± SD)	Controls (Mean ± SD)	
Male:Female	59.04 ± 12.4	54.32 ± 10.02	0.10

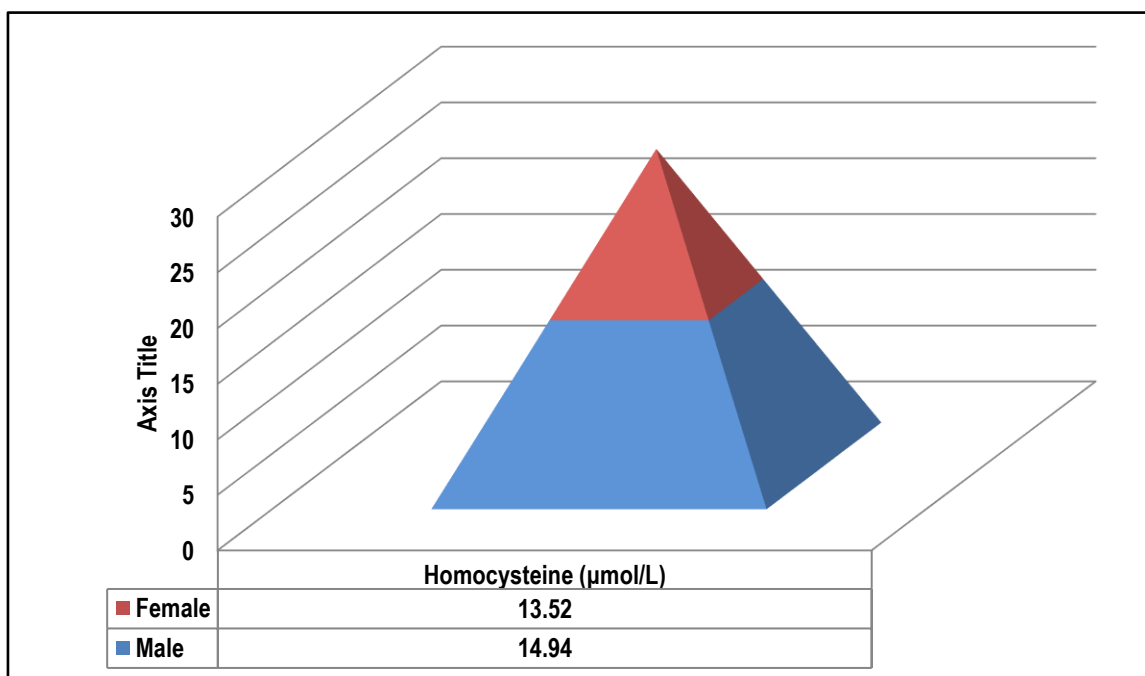


Fig.1: Sex wise distribution of levels of Homocysteine in study group.

Table 2: Level of different biochemical parameters in both study group and control group:

Biochemical Parameters	Cases	Control
Blood Sugar (R) (mg/dl)	117.24±44.21	85.54±16.37
Creatinine (mg/dl)	1.12±0.47	1.02±0.31
Total Cholesterol (mg/dl)	187.4±44.02	142.34±27.02
Triglycerides (mg/dl)	124.51±79.62	96.25±32.24
HDL (mg/dl)	41.23±12.42	49.34±9.28
Homocysteine(μmol/L)	14.98±5.06	11.6±4.26

Statistically significant at $p < 0.05$.

DISCUSSION

Homocysteine is a thiol-containing amino acid derived from methionine or cysteine disulphides (20-30%) or bound to plasma proteins (70-80%). Together, these account for total plasma homocysteine. Homocysteine is postulated to cause ischaemic CVA via various mechanisms, including damaging the vascular matrix, increasing oxidative injury to arterial endothelium, and enhancing proliferation of vascular smooth muscles⁸, but such claims have been refuted by multiple studies.⁹ Increasing age and male sex is associated with higher total homocysteine concentrations.¹⁰ The difference between the sexes could be due to large muscle mass in men since the formation of muscle is associated with the simultaneous formation of homocysteine in connection with creatine/creatinine synthesis.¹¹ The increase in plasma homocysteine may also be due to the influence of sex hormones.¹² The concentrations of total homocysteine was significantly higher in study group than in controls. Further, patients with cerebrovascular accident had elevated levels of blood sugar and serum cholesterol with low HDL-cholesterol. These observations are consistent with that of Tanne et al.¹³ Kam et al¹⁴, also found a strong association between plasma total homocysteine and atherothrombotic disease, which is consistent with our findings. Epidemiological studies have demonstrated that hyperhomocysteinemia is an independent risk factor for stroke.¹⁵ However, the molecular mechanism by which homocysteine promotes atherothrombosis is unknown. Experimental evidence suggests that atherogenic propensity associated with hyperhomocysteinemia results from endothelial dysfunction. Endothelial cell injury, platelet activation, deleterious effect on thrombomodulin expression, protein C activation, and an increased oxidizability of LDL have been described as a few possible mechanisms by which homocysteine provokes arteriosclerosis and thrombosis.¹⁶ 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.¹⁷ Measurement of homocysteine may become an integral part of workup of stroke patients in future.

CONCLUSION

These findings suggest that total homocysteine level is significantly higher in patients with stroke (cerebral infarction) than healthy controls. Now a days, hyperhomocysteinemia is considered an independent risk factor for the incidence of stroke, even though there is lack of convincing explanation till date. It is

therefore important to use serum homocysteine level as an important tool to investigate all cases of cerebrovascular accidents and also in those who are at risk of developing stroke.

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