

TO STUDY THE HOMOCYSTEINE LEVELS IN PATIENTS OF CEREBRAL VASCULAR ACCIDENTSRanjeet Kaur¹, Gurinder Mohan², Jang Bahadur Singh³**HOW TO CITE THIS ARTICLE:**

Ranjeet Kaur, Gurinder Mohan, Jang Bahadur Singh. "To Study the Homocysteine Levels in Patients of Cerebral vascular Accidents". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 29, July 21; Page: 8090-8094, DOI: 10.14260/jemds/2014/3017

ABSTRACT: BACKGROUND: Stroke is the second most common cause of death and major cause of disability worldwide. Plasma homocysteine concentration is one of the emerging modifiable risk factor for stroke. The objective of this study was to evaluate the fasting homocysteine levels in different type of stroke (ischemic and hemorrhage). **MATERIAL AND METHODS:** The present study was a case control study in which fifty patients with the diagnosis of stroke (intracerebral infarct and hemorrhage) were enrolled and fasting serum homocysteine were measured in all and its comparison was done with 25 healthy controls. **RESULT:** Out of total 50 patients of stroke 41(82%) had intracerebral infarct & 9(18%) had intracerebral hemorrhage. In stroke patients 32(64%) had raised serum homocysteine levels, which was significantly higher than that of control group 2 (8%) [p < 0.001]. However there was no significant difference of homocysteine levels between intracerebral infarct 26(63%) and intracerebral hemorrhage 6(66%) [P=0.854]. There were no significant relationships of raised serum homocysteine levels with hypertension, diabetes; LDL levels with the above mentioned stroke risk factors except for smoking (33.14±19.02). Two patients had died during hospital stay and one of them had raised serum homocysteine levels [P=0.64]. **CONCLUSION:** The present study concluded that hyperhomocysteinaemia seems to be a factor for stroke (both in intracerebral infarct and hemorrhage), in addition to conventional risk factors. No significant difference of serum homocysteine existed between intracerebral infarct and hemorrhage. It is concluded that fasting serum homocysteine levels should be assessed in all patients with first episode of stroke.

INTRODUCTION: Stroke is a global health problem and is a leading cause of adult disability.¹ Of 35 million deaths attributable to chronic non communicable diseases that occurred worldwide in 2005, stroke was responsible for 5.7 million (16.6%) deaths, and 87% of these deaths occurred in low-income and middle-income countries.²

The traditional definition of stroke, devised by the World Health Organization in the 1970s,³ is a "neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours". WHO report found hypertension, diabetes mellitus, smoking, hyperlipidemia to be risk factors for stroke in India.⁴

At present, only about two thirds of all strokes can be attributed to known causal risk factors. A previously unrecognized risk factor for stroke, which is prevalent and modifiable, is elevated plasma homocysteine.⁵ Hyperhomocysteinemia appears to act independently of other risk factors. Low serum folate levels are often associated with high homocysteine levels.⁶

A key early event in homocysteine-mediated vascular damage is endothelial injury through direct toxicity and apoptosis,⁷ and endothelial dysfunction resulting in impaired endothelium-

dependent dilatation of blood vessels combined with a proinflammatory and proatherosclerotic endothelial phenotype.⁸

AIMS AND OBJECTIVES:

1. To detect relationship between fasting homocysteine level in different type of cerebrovascular accidents i.e. ischaemic and haemorrhagic stroke.
2. To assess conventional risk factors for stroke (hypertension, diabetes mellitus, dyslipidemia, and smoking) and to correlate their relationship with homocysteine levels in stroke.

MATERIAL AND METHODS: The present case control study was carried out in fifty patients of stroke (intracerebral infarct and hemorrhage) admitted in emergency, ICU and medical wards of Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. These were compared with twenty five age and sex matched healthy individuals visiting the OPD randomly selected to serve as controls.

Those cases with first ever episode of stroke and presented within 24 hours of onset of symptoms were included in the study.

Patients with the following concomitant illnesses like - previous history of ischemic or valvular heart disease, past history of stroke, peripheral vascular disease, hypothyroidism, epilepsy, renal impairment, drugs that affect homocysteine, Vit B₁₂, Folate metabolism i.e. fibrates, statins and niacin, methotrexate and sulfasalazine, anticonvulsant drugs, and levodopa, oral contraceptives, pregnancy, anticoagulant therapy and hypercoagulable state/ coagulopathy/ anticoagulant therapy were known to elevate serum homocysteine were excluded from the study.

RESULTS: A descriptive study was performed with aim to study the relationship of fasting homocysteine levels and stroke and to correlate relationship of homocysteine with conventional risk factors. Detailed history and general physical examination along with systemic examination and necessary investigation was carried out in each case. Fasting serum homocysteine was estimated by Microplate enzyme immunoassay method in all the patients of stroke within 24 hour of presentation and controls.

The mean age of patients was 62.48 ± 11.25 years, maximum number of cases (40%) were in 61-70 year age group. Incidence of stroke was more in males (64%) as compared to females (36%), with male: female ratio of 1.7:1. 41(82%) patients had intracerebral infarct and 9 (18%) patients had intracerebral hemorrhage.

Hypertension as a risk factor was present in 37 (74%) cases of stroke. 30 (73%) of intracerebral infarct patients had hypertension as a risk factor, and 7 (77%) patients of intracerebral hemorrhage had hypertension as a risk factor for stroke. Out of 37 patients of hypertension, 24(75%) had raised serum homocysteine levels. While out of 13 normotensive patients of stroke 8(61%) had raised serum homocysteine levels [P =0.83], indicating hyperhomocystienemia is unrelated to the independent presence or absence of hypertension.

Diabetes mellitus as risk factor was present in 15 (30%) patients of stroke. Diabetes mellitus as risk factor was present in 13 (31.7%) in intracerebral infarct and 2 (22%) in patients of intracerebral hemorrhage. Out of 15 diabetic patients, 8(53%) had raised serum homocysteine levels.

In non-diabetic 24 (68%) had raised serum homocysteine levels [P=0.304], indicating that hyperhomocystienemia is independent risk factor for stroke irrespective of presence or absence of diabetes.

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7(14%) patients had history of smoking and all of them had intracerebral infarct. Mean serum homocysteine levels in patients with history of smoking was 33.14 ± 19.02 . While in non-smoker the mean serum homocysteine levels was 20.09 ± 10.90 [$P=0.012$], indicating smoking as independent risk factor for stroke.

RISK FACTORS	INTRACEREBRAL INFARCT (n=41)	INTRACEREBRAL HAEMORRHAGE (n=9)
HYPERTENSION	30(70%)	7(77%)
DIABETES MELLITUS	13(31%)	2(22%)
SMOKING	7(17%)	0(0%)

TABLE 1: COLLECTIVE DISTRIBUTION OF RISK FACTORS IN DIFFERENT TYPE OF STROKE

Hypertension was most common risk factor in stroke (intracerebral infarct and hemorrhage) followed by diabetes mellitus and smoking.

SERUM HOMOCYSTEINE LEVELS	CASES (n=50)	CONTROLS (n=25)	TOTAL
RAISED (>15)	32	2	34
NOT RAISED (< 15)	18	23	41
TOTAL	50	25	75

TABLE 2: CO-RELATION OF SERUM HOMOCYSTEINE BETWEEN CASES AND CONTROL

Serum homocysteine levels were highly significantly raised in cases of stroke when compared with control patients.

	INTRACEREBRAL INFARCT(n=41)	INTRACEREBRAL HAEMORRHAGE(n=9)
RAISED (> 15)	26(63%)	6(66%)
NORMAL (< 15)	15(36%)	3(33%)
TOTAL	41	9

TABLE 3: CO-RELATION OF SERUM HOMOCYSTEINE LEVELS WITH TYPE OF STROKE

Serum homocysteine levels were not significantly raised when different types of stroke (intracerebral infarct and hemorrhage) were compared.

DISCUSSION: Homocysteine is a sulfhydryl amino acid that is readily oxidized to homocysteine and homocysteine-cysteine mixed disulfide in the plasma. Homocysteine refers to the sum of homocysteine, homocysteine, and the homocysteine-cysteine mixed disulfide, in both the free and protein-bound forms. Deficiencies of the vitamins folic acid (B_9), pyridoxine (B_6), or B_{12} (cobalamin) can lead to elevated homocysteine levels.⁹

An ideal homocysteine level is less than 9 mol/L. Hyperhomocysteinaemia is term used for elevated levels of homocysteine in plasma i.e. greater than 14 mol/L.

In present study was performed to correlate levels of serum homocysteine in patients presenting within 24 hrs of acute stroke (intracerebral infarct and hemorrhage) our main

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observation was that serum homocysteine was significantly raised in patients of stroke when compared with control. According to different Indian studies serum homocysteine was significantly raised in ischemic stroke. In contrast our study did not show any significant correlation with raised serum homocysteine in both intracerebral infarct and intracerebral hemorrhage.

Brattstorm et al¹⁰ in their study concluded that hyperhomocysteinaemia is frequently present in cases of stroke and is independent of other stroke risk factors (hypertension, smoking, or dyslipidemia, or to the concentrations of blood glucose). Raised serum homocysteine levels were independent of conventional risk factors for stroke i.e. hypertension, diabetes mellitus, raised LDL.

Una B. Fallon et al¹¹ examined the association between total serum homocysteine concentration and cerebral infarction in smokers. They observed that smoking was one of the independent risk factor for ischemic stroke. In our study stroke patients with history of smoking had higher serum homocysteine levels.

In our study, hypertension was major risk factor for stroke followed by raised LDL, diabetes mellitus and smoking respectively. No significant difference of serum homocysteine was observed in male and female population.

SUMMARY AND CONCLUSIONS: In conclusion, the present study suggest that hyperhomocysteinaemia seems to be an independent risk factor for stroke (both in intracerebral infarct and hemorrhage), in addition to conventional risk factors, although the prognosis of stroke probably does not depend on serum homocysteine concentration. No significant difference of serum homocysteine existed between intracerebral infarct and hemorrhage, probably because of lesser number of patients with intracerebral hemorrhage in our study. It is concluded that fasting serum homocysteine levels should be assessed in all patients with first episode of stroke.

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Date of Submission: 10/07/2014.

Date of Peer Review: 11/07/2014.

Date of Acceptance: 15/07/2014.

Date of Publishing: 17/07/2014.