



Serum Homocysteine Levels in Hypertensive & Diabetic Patients

KEYWORDS

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ABSTRACT *Introduction:* Stroke is a common worldwide health problem. It is one of the major cause of morbidity, mortality and disability in developed as well as developing countries after coronary artery disease. Recent findings suggest that laboratory testing for plasma homocysteine levels can improve the assessment of risk factors such as hypertension and elevated cholesterol in stroke patients. It has been estimated that full implementation of currently available preventive strategy could reduce stroke incidence by as much as 50 - 80 %. So the purpose of the study was to study serum homocysteine levels in stroke patients with hypertension and diabetes. **Materials and Methods :** 40 patients of cerebrovascular accidents admitted to Hospital. The study was carried out in patients admitted with focal neurological deficit over a period of 2 years. Serum homocysteine was estimated by enzymatic photometry method. **Observations and Results :** In this study of 40 patients presenting with neurological deficits due to cerebrovascular accidents, it was observed that mean serum homocysteine levels were higher in hypertensive patients than in normotensive patients. But there was not much difference in the serum homocysteine levels between the diabetic and non diabetic patients. **Conclusion ;** The present study revealed that hyperhomocysteinemia appears to be an important risk factor for stroke especially those with hypertension than diabetes.

Introduction: Stroke is a common worldwide health problem. It is one of the major cause of morbidity, mortality and disability in developed as well as developing countries after coronary artery disease¹.

There are many risk factors for stroke including age, sex, family history of stroke, hypertension, smoking, diabetes, obesity, hyperlipidemia and atrial fibrillation. Many studies indicate a plethora of conventional risk factors for stroke. Nevertheless, cerebrovascular events do occur sometimes in the individuals without any of the previously mentioned risk factors. As a consequence, it is very likely that other risk factors exist. Identification of modifiable risk factors for stroke may lead to more effective prevention of first and recurrent episodes of cerebrovascular disease.²

Hyperhomocysteinemia causes increased arterial blood pressure thereby increasing the risk of cerebrovascular accidents. Elevated plasma homocysteine has also been shown to induce oxidative injury to vascular endothelial cells and cause impairment of the endothelial production of nitric oxide, a strong vascular relaxing factor.^{4,5,6} Other proposed mechanisms include enhancement of platelet adhesion to endothelial cells, promotion of the growth of vascular smooth muscle cells and association of increased homocysteine with higher levels of prothrombotic factors such as -thromboglobulin, tissue plasminogen activator and factor VIIc³.

Homocysteine is an amino acid in the blood. It is not obtained from the diet and is biosynthesized from methionine via multi step process.

Plasma homocysteine levels are strongly influenced by diet, as well as by genetic factors. The dietary components with the greatest effects are folic acid and vitamins B₆ and B₁₂. Folic acid and other B vitamins help break down homocysteine in the body. Several studies have found that higher blood levels of B vitamins are related, at least part-

ly, to lower concentrations of homocysteine.^{7,8,9} Other recent evidence shows that low blood levels of folic acid are linked with a higher risk of fatal coronary heart disease and stroke.

Several clinical trials are under way to test whether lowering homocysteine will reduce coronary heart disease risk. Recent data show that the institution of folate fortification of foods has reduced the average level of homocysteine in the United States population. Recent findings suggest that laboratory testing for plasma homocysteine levels can improve the assessment of risk. It may be particularly useful in patients with a personal or family history of cardiovascular disease, but in whom the well-established risk factors (smoking, high blood cholesterol, high blood pressure) do not exist.

Although evidence for the benefit of lowering homocysteine levels is lacking, patients at high risk should be strongly advised to be sure to get enough folic acid and vitamins B₆ and B₁₂ in their diet. Foods high in folic acid include green leafy vegetables and grain products fortified with folic acid. But this is just one of the risk factor. A physician taking any type of nutritional approach to reducing risk should consider a person's overall risk factor profile and adjust the diet accordingly

The reason for the decline in the incidence of major stroke in recent years are unclear, may be due to the treatment of risk factors such as hypertension and elevated cholesterol.^{10,11} It has been estimated that full implementation of currently available preventive strategy could reduce stroke incidence by as much as 50 - 80 %. So the purpose of the study was to study serum homocysteine levels in hypertensive and diabetes patients.

Materials and Methods

All patients of cerebrovascular accidents admitted to Sree Balaji Medical College and Hospital, Chrompet over a pe-

riod of 2 years.

Prior to admission to the study, a detailed history was taken and a thorough physical examination was performed so as to fulfil the inclusion and exclusion criteria laid down in the study protocol. The ethical committee of the college cleared the study.

Serum homocysteine was estimated by enzymatic photometry method. Enzymatic photometry is a technique used for estimation of the concentration of a substance by exploiting the property of absorption of light of a particular wavelength. To be more precise, photometry is used to determine the concentration of a light-absorbing compound present in a solution. 4 ml blood was collected from the patient and serum was separated immediately for the analysis.

Observations and Results

In this study of 40 patients presenting with neurological deficits due to cerebrovascular accidents, 24 male patients and 16 female patients were studied. In the present study, it was observed that according to age and sex wise distribution of patients male patients were of younger age as compared to female patients. It was observed that Mean serum homocysteine levels were higher in male patients than females. However the difference was statistically not significant ($p > 0.05$). Mean serum homocysteine levels were higher in smokers than non-smokers. The difference was not statistically significant ($p < 0.05$).

Table 1 : Independent samples T-Test to compare mean S. Homocysteine ($\mu\text{mol/L}$) levels between HTN and Normal

	HTN	N	Mean	Std. Dev
S.HOMOCYSTEINE LEVELS ($\mu\text{mol/L}$)	No	12	19.33	7.364
	Yes	28	29.26	15.957

Mean serum homocysteine levels were higher in hypertensive patients than in normotensive patients. The difference was statistically significant ($p < 0.05$).

Table 2: Independent samples T-Test to compare mean S. Homocysteine ($\mu\text{mol/L}$) level between DM and Normal

	DM	N	Mean	Std. Dev
S. HOMOCYSTEINE LEVELS ($\mu\text{mol/L}$)	No	31	26.34	15.159
	Yes	9	26.11	13.252

There was not much difference in the serum homocysteine levels between the diabetic and non diabetic patients. The difference was statistically not significant ($p > 0.05$).

Discussion

Many studies have showed that ^{12,13,14} increased homocysteine represents an independent risk factor for coronary, cerebrovascular and peripheral arterial disease. Various risk factors for cerebrovascular accidents like age, sex, food habit, hypertension, diabetes mellitus and lifestyle were studied and analyzed in relation to serum homocysteine levels.

Hyperhomocysteinemia is one of the newly recognized factor that increases 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. Measurement of homocysteine may become the integral part of workup of stroke patients in future.

In this study of 40 patients, 17 patients were less than 60 years and 23 patients were more than 60 years of age. It was also observed that patients less than 60 years had a mean homocysteine of 29.43 where as those more than 60 years had a mean homocysteine level of 30.45. However, the difference was statistically not significant ($p > 0.05$). Our findings were consistent with other studies ^{12,13,14}.

However, according to study findings of Mudd SH et al and Mc Cully KS ^{16,17} increase in the serum homocysteine levels were observed with increasing age.

Our study comprised of 24 (60%) male patients and 16 (40%) female patients. Mean serum homocysteine levels were higher in males (29.21) than females (21.89). However, the difference was statistically not significant ($p > 0.05$). Our findings were consistent with study of Narang et al, Modi et al, Bogdan et al⁵ and Andrew et al^{6,9,19}.

However Kang et al studies shows that young healthy women have homocysteine levels lower than healthy men. This difference diminishes with ageing. An abrupt increase in serum homocysteine in women after 50 years suggests that sex difference in homocysteine disappears with increasing age ²⁰.

Our study consisted of 20 (50%) smokers and 20 (50%) non-smokers. Mean serum homocysteine levels in smokers was higher (29.43) than non-smokers (23.14). The difference was not statistically significant ($p < 0.05$). Our results were similar to findings ^{18,19,20} reported significant relationship between smoking and serum homocysteine levels.

In our study, 28 (70%) patients were hypertensives and 12 (30%) were normotensives. Mean serum homocysteine levels were higher in hypertensive patients (29.26) than normotensive patients (19.33). The difference was not statistically significant ($p < 0.05$). Our results were similar to findings ^{17,18,19} found definite evidence of an increased homocysteine in hypertensive patients.

In our study, 9 (22.5%) patients belonged to diabetic group and 31 (77.5%) patients belonged to non diabetic group. Mean and Standard deviation of serum homocysteine levels were 26.11 and 13.252 in diabetic group and 26.34 and 15.159 in non diabetic group. The difference was statistically not significant ($p > 0.05$). Our findings were consistent with study.^{21,22,23}

In conclusion the present study revealed that hyperhomocysteinemia appears to be an important risk factor & therefore important to use serum homocysteine level as an important tool to investigate in all cases of hypertension.

References :

1. Dutta S, Pal SK, Mazumdar H et al. Homocysteine and cerebrovascular accidents. *J Indian Med Assoc* 2009 June;107(6):345-6.
2. Peter Rothwell. Cerebrovascular diseases. In: Michael Donarghy, editor. *Brain's diseases of the nervous system*. 12th ed, New York: *Oxford University Press*: 2009. p. 1003-16.
3. Susan Standing. *Gray's anatomy The anatomical basis of clinical practice*. 40th ed, Newyork: Elsevier Churchill livingstone; 2008. p.227,253
4. Longo DL, Fauci AS, Kasper DL et al, editors. *Harrison's principles of internal medicine*. 18th ed. New York: *Mc Grath Hill*; 2011.
5. Bogdan N Manolescu, Eliza Opera, Ileana C Farcasanu et al. Homocysteine and vitamin therapy in stroke prevention and treatment: a review. *Acta Biochimica Polonica* 2010;57(4):467-77.
6. Roudbari SA, Amini A. Survey homocysteine serum level in CVA ischemic infarct patients. *Journal of Guilan University of Medical Sciences fall* 2006;15(59):20-25.
7. Zongte Z, Shaini L, Gyaneshwar WS et al. Serum homocysteine levels in cerebrovascular accidents. *Indian J of Clinical Biochemistry* 2008;23(2):154-7.
8. Nagaraja D, Christopher R. Homocysteine and stroke. *Ann Indian Acad Neurol* 2004;7:357-67.
9. Elise N Rowan. Homocysteine and post-stroke cognitive decline. In: Elise N Rowan, Heather O Dickinson, Sally Stephens et al. *Poster at Autumn Meeting of the British Geriatrics Society* 2005;339-43.
10. Mcllroy SP, Dynan KB, Lawson JT et al. Moderately elevated plasma homocysteine, methylenetetrahydrofolate reductase genotype and risk factor for stroke, vascular dementia and Alzheimer disease in Northern Ireland. *Stroke* 2002;33:2351-6.
11. Bots ML, Launer LJ, Lindemans J et al. Homocysteine and short-term risk of myocardial infarction and stroke in the elderly. *The Rotterdam Study. Archives of Internal Medicine* 1999;159:38-44.
12. Seshadri S, Beiser A, Selhub J et al. Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *New England Journal of Medicine* 2002;346:476-83.
13. Olusegun AM, Marouf R, Abdel RA et al. Determinants and associations of homocysteine and prothrombotic risk factors in Kuwaiti patients with cerebrovascular accidents. *Med Princ Pract* 2008;17:136-42.
14. Woo KS, Chook P, Lolin YI et al, Hyperhomocyst(e)inemia Is a Risk Factor for Arterial Endothelial Dysfunction in Humans. *Circulation* 1997;96:2542-44.
15. Perry IJ. Homocysteine, hypertension and stroke. *Journal of Human Hypertension* 1999;13:289-93.
16. Mudd SH et al. The natural history of homocystinuria due to cystathionine beta- synthase deficiency. *Am J Hum Genet* 1985;37:1-31.
17. Mc Cully KS. Vascular pathology of homocysteinemia: implications for the pathogenesis of atherosclerosis. *Am J Pathol* 1969;56:111-28.
18. Graham MI, Leslie E D, Refsum H et al. Plasma Homocysteine as a risk factor for vascular disease: The European concerted action project. *JAMA* 1997;277(22):1775-82.
19. Andrew G, Boston MD, Irwin H et al. Non fasting plasma total homocysteine levels and stroke incidence in elderly persons. *Ann Intern Med*. 1999;131:352-55.
20. Boysen G, Brander T, Christens H et al. Homocysteine and Risk of Recurrent Stroke. *Stroke* 2003;34:1258-61.
21. Kelly PJ, Furie KL, Kistler JP et al. Stroke in young patients with hyperhomocysteinemia due to cystathionine beta-synthase deficiency. *Neurology, American Academy of Neurology* 2003 Jan 28;60(2):275-9.
22. Kristensen B, Malm J, Nilsson TK et al. Hyperhomocysteinemia and Hypofibrinolysis in Young Adults With Ischemic Stroke. *Stroke* 1999;30:974-80.
23. Woo KS, Chook P, Lolin YI et al, Hyperhomocyst(e)inemia Is a Risk Factor for Arterial Endothelial Dysfunction in Humans. *Circulation* 1997;96:2542-44.