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Estimation of Serum Homocysteine Levels in Cerebrovascular Accidents: Cross Sectional Study

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ABSTRACT

The present study was performed to determine serum homocysteine levels in cerebrovascular accidents. The aim and objective were to study serum homocysteine levels as risk factor for cerebrovascular accident. The study was restricted to patients admitted to Sri Balaji Medical College and Hospital, Chrompet with focal neurological deficit due to cerebrovascular accidents. Neurological deficit due to other causes were excluded. All the patients were subjected to thorough history, clinical examination and investigations including fasting lipid profile, CT scan brain and serum homocysteine. Our mam observation was that serum homocysteine levels were elevated m cerebrovascular accident patients significantly, both in cases of infarct and hemorrhage.

Key words: Homocysteine, Strokes, Hemorrhage, Vascular origin, Sinuses

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INTRODUCTION

Stroke is a common worldwide health problem. It is one of the major causes of morbidity, mortality and disability in developed as well as developing countries after coronary artery disease [1]. There are about one million strokes in the European Union every year, making it by far the most common neurological disorder. After coronary artery disease and cancers, stroke is the third common cause of death in the world, causing about 4 million deaths in 1990, and three quarters of them in developing counts. A Stroke (previously known as cerebrovascular accident) is rapidly developing clinical symptoms and/or signs of focal and at times global (applied to patients in deep coma and those with subarachnoid hemorrhage) loss of brain function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin. There is a wide range of severity, from recovery 1n few days, through persistent disability, to death [2]. Mortality due to stroke rapidly with age [1-3]. The burden of stroke components largely of the elderly population.

However, there remains a small but significant subset of younger patients with ischemic stroke, in whom conventional vascular risk factors play a smaller role. About 85% of all strokes are ischemic, 10% are due to primary intracerebral hemorrhage and about 05% are due to subarachnoid hemorrhage. Among the Ischemic stroke, 25% are caused by large artery disease, 25% by small vessel disease, 20% by cardiac embolism, 05% by other rare causes [2]. The brain is a highly vascular organ, its profuse blood supply characterized by a densely branching arterial network. It has a high metabolic activity due in part to the energy requirements of constant neural activity [4]. It demands about 15% of the cardiac output and utilizes 25% of the total oxygen consumption of the body. The brain is supplied by two internal carotid arteries and two vertebral arteries which form a complex anastomosis (circulus arteriosus, circle of Willis) on the base of the brain. Vessels diverge from this anastomosis to supply the various cerebral regions. In general, the internal carotid arteries

and the vessels arising from them supply the forebrain, with the exception of the occipital lobe of the cerebral hemisphere, whereas the vertebral arteries and their branches supply the occipital lobe, the brain stem and the cerebellum. Venous blood from the brain drains into sinuses within the dura mater. Acute interruption of the blood supply to the brain for more than a few minutes causes permanent neurological damage. Such ischemic strokes along with intracranial hemorrhage are major contemporary sources of morbidity and mortality [3]. The definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. The diagnosis of stroke (versus not stroke) is still a matter of clinical skill often without the help of many, or any, confirmatory investigations. However, this does have the advantage that the diagnosis is independent of the availability and quality of rapidly changing technology (such as CT scanners), which is often not available at all in developing countries, or even universally available in developed countries4 Once the diagnosis of stroke is made, brain imaging studies are needed to determine if the cause of stroke is ischemia or hemorrhage. The clinical manifestation of stroke is highly variable because of the complex anatomy of the brain and its vasculature. There are several common causes of sudden onset neurologic symptoms that May m1m1c stroke, including seizure, intracranial tumor, migraine, and metabolic encephalopathy [5,6].

A fall in cerebral. blood flow to zero causes death of brain tissue within 4-10 minutes; values <16-18 ml/I 00 gm tissue per minute cause infarction within an hour; and values <20 ml/I 00 gm tissue per minute cause ischemia without an infarction unless prolonged for several hours or days. Neurologic symptoms manifest within seconds because neurons lack glycogen, so energy failure is rapid. If the cessation of blood flow lasts more than a few mi nutes , infarction or death of brain tissue results. The standard definition of Transient Ischemic Attack (TIA) requires that all neurologic signs and symptoms resolve within 24 hours regardless of whether there is imaging evidence of new permanent injury; stroke has occurred if the neurologic signs and symptoms lasts for >24 hours [7,8].

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. Therefore, 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. Hyperhomocysteinemia, defined as an elevated plasma total homocysteine concentration (>IO μM), is one such modifiable risk factor [9].

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. 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 VIie. Homocysteine is an amino acid in the blood. It is not obtained from the diet and 1s 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 B 6 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 partly, to lower concentrations of homocysteine. 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 [10-13].

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's high in folic acid includes green leafy vegetables and grain products fortified with folic acid. But this is just one of the risk factors. 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 [14]. 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. It has been estimated that full implementation of currently available preventive strategy could reduce stroke incidence by as much as 50-80%.

MATERIALS AND METHODS

Source of data

All patients of cerebrovascular accidents admitted to Sri Balaji Medical College and Hospital, Chrompet over a period of 2 years.

Methods of collection of data

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. The study was carried out in patients admitted with focal neurological deficit to Sri Balaji Medical College and Hospital, Chrompet over a period of 2 years.

Inclusion criteria

All the patients admitted to Sri Balaji Medical College and Hospital, Chrompet with focal neurological deficit due to suspected Cerebrovascular accident.

Exclusion criteria

All the patients admitted to Sri Balaji Medical College and Hospital, Chrompet with neurological deficit due to causes other than Cerebrovascular accident.

Method of estimation of homocysteine

Serum homocysteine was estimated by enzymatic photometry method. Enzymatic photometry 1s 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. Whenever a light of wavelength enters a solution or a substance, it comes out with a reduced intensity. This is because a part of it is absorbed by the solution. If this property needs to be exploited for the analytical work or biochemical assay, the phenomenon of absorption of light should obey the Beer-Lambert's Law. By combining both the laws, it can be stated that the intensity or amount of light decreases exponentially with the increase in the concentration of the solution and the depth or thickness of the solution through which the light passes.

Analyzers used

Olympus AU 2700 Modular E 170, Roche P 800.

Sample taken

4 ml blood was collected from the patient and serum was separated immediately for the ana1ysis.

RESULTS

In this study of 40 patients presenting with neurological deficits due to ce rebro vascular 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 (Figure 1).

From the Table 1, it is 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 2 and Figure 2).

Mean serum homocysteine levels were higher in patients with sedentary lifestyle than in patients with active lifestyle. The difference was statistically highly significant ($p < 0.01$) (Table 3).

Mean serum homocysteine levels were higher in patients on vegetarian diet than in patients on mixed diet. However statistical significance could not be established ($p > 0.05$) (Table 4).

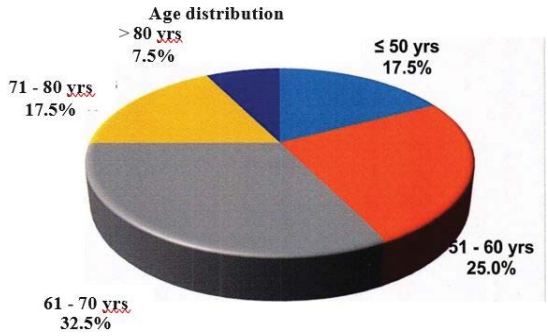

Figure 1: Age wise distribution of patients.

Table 1: Independent samples T-Test to compare mean S. Homocysteine (µmol/L) level between genders.

	Gender	N	Mean	Std. Dev
S. Homocysteine levels (µmol/L)	Male	24	29.21	16.218
	Female	16	21.89	10.757

Table 2: Independent samples T-Test to compare mean S. Homocysteine (µmol/L) level between smokers and non-smokers.

	Smoking	N	Mean	Std. Deviation
S. Homocysteine levels (µmol/L)	No	20	23.14	13.244
	Yes	20	29.43	15.51

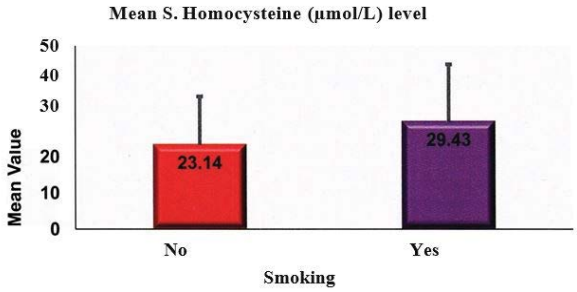

Figure 2: Comparison of serum homocysteine level with smoking habit.

Table 3: Independent samples T-Test to compare mean S. Homocysteine (µmol/L) level between sedentary and non-sedentary.

	Lifestyle	N	Mean	Std. Dev
S. Homocysteine levels (µmol/L)	Sedentary	34	28.46	14.703
	Non-sedentary	6	13.98	4.382

Table 4: Independent samples T-Test to Compare mean S. Homocysteine (µmol/L) level between Veg and mixed diet.

	Diet	N	Mean	Std. Dev
S. Homocysteine Levels (µmol/L)	Veg	3	34 .00	20 . 522
	Mi xed	37	25 .66	14 .205

Table 5: Comparison between mean S. Homocysteine (µmol/L) level and CT scan results.

CT scan	N	Mean	Std. Dev
Normal	4	13.96	3.785
Infarct	34	26.93	14.383
Haemorrhagic	2	39.99	20.789
Total	40	26.28	14.588

Mean serum homocysteine levels were higher in patients with infarct than in patients with normal CT finding. Mean serum homocysteine levels were higher in patients with hemorrhage than in patients with normal CT finding. Mean serum homocysteine levels were higher in patients with hemorrhage and infarct taken together than in patients with normal CT finding (Table 5 and Figure 3).

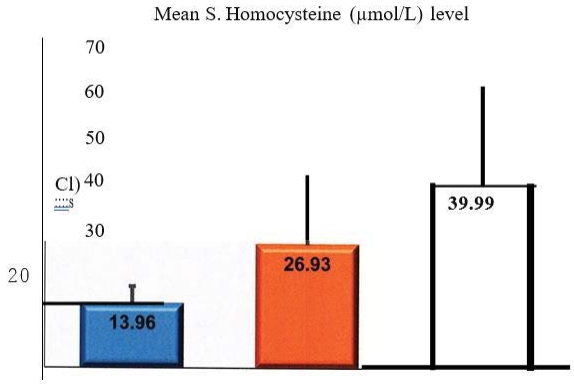

Figure 3: Comparison of serum homocysteine Level with CT finding.

DISCUSSION

Many studies have showed that 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,diabetesmellitusandlifestyle were studied and analyzed in relation to serum homocysteine levels. Hyperhomocysteinemia is one of the newly recognized factors that mcreases the risk 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 an integral part of workup of stroke patients in future [15].

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 whereas those more than 60 years had a mean homocysteine level of However, the difference was statistically not significant (p > ef:"05). Our findings were consistent with previous studies. However, according to findings of Longo et al. [4] and Zongte et al. [6] increase in the serum homocysteine levels were observed with increasing age. Our study comprised of 24 (60%) male patients and 16 (40%) female 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 study consisted of 10 (25%) patients with stroke recurrence and 30 (75%) patients with new onset stroke (first time stroke). Mean and Standard deviation of serum homocysteine levels were 22. 76 and 10. 521 in stroke recurrence group and 27.46 and 15,688 in new onset stroke group. The difference was statistically not significant (p >0.05). However, previous studies 73 reported significantly higher serum homocysteine levels in recurrent stroke patients. Previous studies found no difference homocysteine between patients who previously had cerebral infarcts and hemorrhage. Our study consisted of 34 (85%) patients with sedentary lifestyle and 6 (15%) patients with active lifestyle. Mean serum homocysteine levels were higher in sedentary lifestyle (28.46) than active, lifestyle (13.98). The difference was statistically highly significant (p <0.01). Rasmussen, et al. suggested association between hyperhomocysteinemia and established vascular risk likely to reflect lifestyle fact [16].

In our study, only 3 (7.5%) patients were on vegetarian diet and 37 (92.5%) patients were on mixed diet. Mean and Standard deviation of serum homocysteine levels were 34 and 20.522 in vegetarians and 25.66 and 14.205 in patients on mixed diet. However, the difference was statistically not significant (p >0.05). The associations between hyperhomocysteinemia and established vascular risk factors are likely to reflect, at least in part, links with common underlying dietary and lifestyle factors a diet

high in saturated fat with inadequate folate intake from fruit and vegetables [17].

In our study, 34 (85%) patients were having infarct, 2 (5%) patients were having hemorrhage and 4 (10%) patients were having normal CT finding. Mean homocysteine levels were higher with infarct (26.93) and hemorrhage (39.99) than in patients with normal CT finding (13.96). The difference was statistically significant with both infarct ($p < 0.01$) and hemorrhage ($p < 0.05$). Our findings were consistent with study of Perry et al. [18,19] where serum homocysteine levels were significantly raised m infarcts when compared to hemorrhage. Paul et al. [20] observed no association between hyperhomocysteinemia and cerebrovascular accidents 75 Boushey and colleagues have reported on a meta-analysis of many observational studies relating total homocysteine concentrations to atherosclerotic vascular disease, of which 11 studies addressed the association between homocysteine and risk of st roke 50 , 9 case-control studies provided support for the hypothesis that homocysteine is an independent risk factor for stroke while 2 prospective studies did not support the study [18-21].

CONCLUSION

Our study of serum homocysteine levels in cerebrovascular accidents is a cross sectional study. The present study was performed to determine serum homocysteine levels in cerebrovascular accidents. The aim and objective were to study serum homocysteine levels as risk factor for cerebrovascular accident. The study was restricted to patients admitted to Sri Balaji Medical College and Hospital, Chrompet with focal neurological deficit due to cerebrovascular accidents. Neurological deficit due to other causes were excluded.

All the patients were subjected to thorough history, clinical examination and investigations including fasting lipid profile, CT scan brain and serum homocysteine. Our mam observation was that serum homocysteine levels were elevated m cerebrovascular accident patients significantly, both in cases of infarct and hemorrhage. Further serum homocysteine levels were higher in patient's sedentary lifestyle, hypertension, and smoking. Serum homocysteine did not show any relation with age, sex, diabetes mellitus and stroke recurrence. People at risk for cerebrovascular diseases such as hypertension, smoking and sedentary lifestyle should be screened for hyperhomocysteinemia. In conclusion the present study revealed that hyperhomocysteinemia appears to be an important risk factor for cerebrovascular accidents. It 1s therefore important to use serum homocysteine level as an important tool to investigate all cases of cerebl'0vascular ace idents and also in those who are at risk of developing stroke.

FUNDING

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ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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