

Prospective study of homocysteine level in cerebrovascular disease in non diabetic patients at tertiary care centre

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Abstract

Introduction: Stroke is one of the major cause of morbidity, mortality and disability all over the world. There are studies which suggests that elevated serum homocysteine is an independent risk factor for stroke. Various factors have been proposed by different studies for this. **Material and methods:** A prospective study was carried on 60 cerebrovascular accident patients over a period of 18 months at Gajra Raja medical college and JAH Group of hospital Gwalior from Jan 2020 to Jun 2021. Clinical information including age, sex, history of current evidence of hypertension (HTN, diabetes Mellitus (DM) , history of cardiac disease, life style, diet pattern, family history of vascular diseases were recorded for all subjects. Serum homocysteine was estimated by enzymatic method. **Results:** In this study of 60 patients with cerebrovascular accidents, 36 were males and 24 were female patients. Most patients were between 4th to 6th decade of life. There was no statistically significant difference between age/sex and stroke with relation to serum homocysteine. There were 18 out of 40 hypertensive patients who had hypertension. The difference was statistically significant (p value <0.05). seventeen out of 43 patients with vegetarian diet had raised homocysteine level, 5 out of other 17 patients were on mixed diet who had raised homocysteine. The difference was statistically significant (p value <0.05). Nineteen out of 39 patients with sedentary lifestyle had raised homocysteine levels and 3 out of 21 with active lifestyle had raised homocysteine levels. The difference was statistically significant (p value <0.05). Eleven patients were smokers. Out of them 04 (06%) had raised homocysteine level and 49 were nonsmoker patient. Among them, 18(30%) had raised homocysteine level. The difference was statistically insignificant. (p value >0.05). Serum homocysteine levels were elevated in cerebrovascular accident patients significantly, both in cases of infarct and hemorrhage. Further serum homocysteine levels were higher in patients with sedentary lifestyle, hypertension, vegetarian and obesity. Serum homocysteine did not show any relation with age, sex, alcohol and smoking. **Conclusion:** Hyperhomocysteinemia is an important risk factor for cerebrovascular accidents. Hence, it should be to investigate all cases of cerebrovascular accidents and also in those who are at risk of developing stroke.

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Introduction

All over the world, stroke is a common health problem. It is a major cause of morbidity, mortality and disability nowadays in developed as well as developing countries[1].

Each year there are about one million cases of stroke in the European Union making it by far the most common neurological disorder[2]. Stroke is the third common cause of death in the world, only next to coronary heart disease and all other cancers.

Stroke (previously known as cerebrovascular accident) is defined as rapidly developing clinical symptoms and/or signs of focal and sometimes global loss of brain function, with symptoms lasting more than one day or leading to death. Severity ranges from recovery in few days, to sometimes persistent disability, to death[2].

Hyperhomocysteinemia, defined as an elevated plasma total homocysteine (Hcy) concentration more than 18 µmol/L, is one such factor[3].

Some studies have shown that elevated serum homocysteine is an independent risk factor for stroke[4]. Hyperhomocysteinemia has also been associated with vascular dementia[5], myocardial infarction[6] and Alzheimer's disease[7]. Hyperhomocysteinemia is common and is

the main prothrombotic factor associated with cerebrovascular accident[8]. It is also an independent risk factor for arterial dysfunction[9]. Elevated plasma homocysteine level has also shown to induce oxidative injury to vascular endothelial cells and cause impairment of the endothelial production of nitric oxide, which is 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 β-thromboglobulin, tissue plasminogen activator and factor VIIc[8].

The main cause of morbidity and mortality in hyperhomocysteinemia patients is progressive premature arteriosclerosis and associated thromboembolic complications. There are widespread arterial focal lesions with fibrous intimal plaques and medial fibrosis with fraying and splitting of the internal elastic membranes in histological sections. Homocysteine or its derivatives causes these changes[10].

Homocysteine is an amino acid, which is not gained from the diet and is biosynthesized from methionine via multi step process. The dietary components which have greatest effects are folic acid , vitamins B₆ and B₁₂ in the body[3].

Material and method

This prospective study was carried on 60 cerebrovascular accident patients over a period of 18 months at Gajra Raja medical college and JAH Group of hospital Gwalior from Jan 2020 to Jun 2021 , with following criteria's.

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Inclusion criterias were cerebrovascular accident patient (Non-diabetic), with age group of 18 years to 60 years and those who are willing to give informed consent. Exclusion criteria were diabetic cerebrovascular accident patients. Clinical information including age, sex, history of current evidence of hypertension (HTN) i.e. systolic blood pressure (SBP) more than 140mmHg and diastolic BP more than 90mmHg, Diabetes Mellitus (DM) with fasting blood glucose more than 7 mmol/l or 126 mg/dl, any history of cardiac disease, information regarding life style, diet pattern, family history of vascular diseases were recorded for all subjects. Serum homocysteine was estimated by enzymatic method (using GenX Homocysteine kit), The upper limit of the manufacturer and the laboratory was 18 μmol/L. Values above 18 μmol/L were accepted as high. Analyzers used was BIO System-BA400.

Normal levels of homocysteine provided with the kit was as 06-22μmol/L for adult male, 03-18μmol/L for adult female and 25μmol/L for elderly >65 years.

Results

In this study of 60 patients presenting with cerebrovascular accidents, 36 patients were males with the mean age of 44.78 years and 24 were female patients with the mean age of 47.18 years (table 1). Most subjects were from age group between 41 to 65 years.

In the present study, male patients were of younger age as compared to female patients. There was no statistically significant difference between age/sex and stroke with relation to serum homocysteine. This study shows that 40 patient had hypertension. Among them, 18(30%) had raised homocysteine level and 20 were normotensive patient among them 4 (06.66%) had raised homocysteine. The difference was statistically significant (p value <0.05) (table 2).

This study shows that 43 patients were taking vegetarian diet. Among them, 17(28.36%) had raised homocysteine level and 17 were on mixed diet. Among them, 5(08.30%) had raised homocysteine. The difference was statistically significant (p value<0.05) (table 3). This study shows that 11 patient were smoker among them 04 (06%) had raised homocysteine level and 49 were nonsmoker patient. Among them, 18(30%) had raised homocysteine level. The difference was statistically insignificant. (p value >0.05) (table 4).

This study shows that 39 patients had sedentary lifestyle. Among them, 19(31.66) had raised homocysteine levels and 21 had active lifestyle. Among them, 03(05%) had raised homocysteine levels. The difference was statistically significant (p value <0.05) (table 5).

A comparative tabulation of various parameters with its impact on homocysteine levels have been given in table 6.

Tables

Table 1: Comparison of serum homocysteine level with age

Age	No of Patients	Mean ± SD of Homocysteine level (μmol/l)	t – test value p – value and significance
Less than 40 years	16	18.41±06.35	t= -1.67 P=0.10 In Significant
41 to 65 years	44	22.44±11.99	
Total	60	21.36±10.87	

Table 2: Comparison of serum homocysteine level with Blood pressure

	No. of Patients	Percentage	Mean ±SD homocysteine level (μmol/l)	t – test value p – value and significance
Hypertensive	40	66.67	24.40 ± 13.01	t= -2.858 p=0.0255 significant
Normotensive	20	33.33	17.48 ±06.60	
Total	60	100		

Table 3: Comparison of serum homocysteine level with diet

Diet	No. of Patients	Percentage	Mean ±SD homocysteine level(μmol/l)	t – test value p – value and significance
Vegetarian	43	71	23.66 ±10.69	t=0.432 p=0.022 significant
Mixed	17	29	18.62 ±11.61	
Total	60	100		

Table 4: Comparison of serum homocysteine level with smoking habit

	No. of Patients	Percentage	Mean ±SD homocysteine level (μmol/l)	t – test value p – value and significance
Smoker	11	19	23.15± 10.82	t=0.602 p=0.550 Insignificant
Non smoker	49	81	20.96± 10.96	
Total	60	100		

Table 5: Comparison of serum homocysteine level with lifestyle

Life style	No. of Patients	Percentage	Mean ±SD homocysteine level (μmol/l)	t – test value p – value and significance
Active	21	35	17.58± 0760	T=2.03 p=0.047 Significant
Sedentary	39	65	23.40 ±12.01	
Total	60	100		

Table 6: Comparing S. Homocysteine level with various parameters

		No of Patients	Percentage	Mean ± SD of Homocysteine level (μmol/l)	Number and Percentage of patients with raised homocystee level	t – test value p – value and significance
Age	< 40 years	16	27	18.41±06.35	03(5%)	P= >.05
	41 to 65 years	44	73	22.44±11.99	19(31.66)	
Sex	Male	36	60	23.22 ± 12.03	14(23.33)	P= >0.05
	Female	24	40	18.57±08.33	08(13.33)	
BMI	Obese	26	43	24.34± 12.04	15(25%)	P= <0.05
	Non obese	34	57	18.08 ±09.44	07(11.66%)	
Blood Pressure	Hypertensive	40	66.67	24.40 ± 13.01	18(30%)	P= <0.05
	Normotensive	20	33.33	17.48 ±06.60	04(06.66%)	

Diet	Vegetarian	43	71	23.66 ±10.69	19(31.66)	P= <0.05
	Mixed	17	29	18.62 ±11.61	03(05%)	
Smoking Habit	Smoker	11	19	23.15± 10.82	04(06%)	P= >0.05
	Non smoker	49	81	20.96± 10.96	18(30.66)	
Life style	Active	21	35	17.58± 0760	03(05%)	P= <0.05
	Sedentary	39	65	23.40 ±12.01	19(31.66)	

Discussion

Many studies have showed that increased homocysteine level represent an independent risk factor for coronary, cerebrovascular and peripheral arterial disease[11]. Various risk factors for cerebrovascular accidents like age, sex, food habit, hypertension, smoking and lifestyle were studied and the serum homocysteine levels were analyzed in different groups.

Hyperhomocysteinemia is one of the newly recognized factor that increases the risk of vascular disease[8]. Mechanisms by which hyperhomocysteinemia increases risk of cerebrovascular accidents are not clear, but several possible mechanisms have been proposed[8].

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[10].

Measurement of homocysteine level may become the integral part of workup of cerebrovascular accident patients in future.

Comparison of serum homocysteine with age

Our study comprised of 60 patients, 16 (26%) patients were <40 years of age and 44(74%) were 41 to 65 years of age. Mean serum homocysteine levels were higher in patients 41 to 65 years of age (22.44 Umol/L) than in patients less than 40 years of age (18.41 Umol/L). However, the difference was statistically not significant ($p > 0.05$). Our results were similar to findings of Narang et al[12], Modi et al[13] and Nigel et al[14].

However, according to findings of Longo et al[15] and Zongte et al[16] increase in the serum homocysteine levels were observed with increasing age.

Comparison of serum homocysteine according to sex

Present study comprised of 36 (60%) male patients and 24 (40%) female patients. Mean serum homocysteine levels were higher in males (23.22 Umol/L) than females (18.57 Umol/L). However, the difference was statistically not significant ($p > 0.05$). Our results were similar to findings suggested by Narang et al[12], Modi et al[13], Bogdan et al[14] and Andrew et al[17]. However, Kang et al[18] and Markaki I et al[19] showed 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.

Comparison of serum homocysteine according to smoking habit

Our study consisted of 11 (19%) smokers and 49(81%) non-smokers. Mean serum homocysteine levels in smokers was higher (23.15 Umol/L) than non-smokers (20.96 Umol/L). The difference was statistically insignificant ($p > 0.05$). Our results were similar to findings of Perry et al[20] and Roudbari et al[21]. They reported no significant relationship between smoking and serum homocysteine levels. This result could be because 40% of cases were females who were nonsmoker.

Comparison of serum homocysteine with blood pressure

In the present study, 40 (66.67%) patients were hypertensive and 20 (33%) were normotensive. Mean serum homocysteine level were higher in hypertensive patients (24.40 Umol/L) than normotensive patients (17.48 Umol/L). The difference was statistically significant ($p < 0.05$). Our results were similar to findings of , Shan Lu et al[22], Wu H et al[23], Sun et al[24], Narang et al[12], Modi et al[13], Graham et al[25], Olusegun et al[8], Nigel et al[26], Nygard et

al[27], Perry et al[20] and Manilow et al[28]. However, Kittner et al[29] did not find definite evidence of an increased homocysteine in hypertensive patients.

Comparison of serum homocysteine in vegetarian diet vs mixed diet patients

Present study comprised of 43 (71%) patients who were on vegetarian diet and 17 (29%) patients who were taking mixed diet. Mean serum homocysteine levels were higher in vegetarian diet patients (23.66 Umol/L) than mixed diet patients (18.62 Umol/L). The difference was statistically significant ($p < 0.05$). Our results were similar to findings of Panagiotakos DB et al[30], Karger AG et al[31], Kalita J et al[32], Bree A et al[33] and L. Bissoli et al[34].

Comparison of serum homocysteine with Life Style

Our study comprised of 21 (35%) patients with active life style and 39 (65%) with sedentary life style. Mean serum homocysteine level were higher in sedentary life style patients (23.40 Umol/L) than active lifestyle patients (17.58 Umol/L). The difference was statistically significant ($p < 0.05$). Our results were similar to findings of Panagiotakos DB et al[30] and Bree AD et al[33].

Comparison of serum homocysteine with body mass index

In our study, 26 (43%) patients were obese and 34(57%) were nonobese. Mean serum homocysteine levels were higher in obese patients (24.34 Umol/L) than non-obese patients (18.80 Umol/L). The difference was statistically significant ($p < 0.05$). Our results were similar to findings of Karatela RA et al[35], Haloum M et al[36], Bree AD et al[33].

Conclusion

Hyperhomocysteinemia is an important risk factor for cerebrovascular accidents. 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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