IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 7 Ser.15 (July. 2021), PP 51-55
www.iosrjournals.org

A Study of Plasma Homocysteine Levels in Ischaemic Stroke.

[1] Dr.R.Vasudev, [2] Dr.Raghavendra Naik M, [3] Dr.Vivek Rayavarapu, [4]Dr.K.Srinivas,

[1]MD General Medicine, Assistant Professor, Department of General Medicine, King George Hospital, Vishakhapatnam, Andhra Pradesh, India
[2]MD General Medicine, Civil Assistant Surgeon Specialist, CHC Nizampatnam, Guntur, Andhra Pradesh, India
[3]MBBS (Research Assistant), NRI Medical College, Vijayawada, Andhra Pradesh, India
[4]Assistant Professor, Department of Pharmacology, Andhra Medical College, Vishakhapatnam, Andhra Pradesh, India
Corresponding author: Dr.K.Srinivas

Abstract
INTRODUCTION*: Increased plasma levels Homocysteine is now considering as individual risk factors for cerebrovascular disease, myocardial infarction, and peripheral arterial occlusive disease. Hyper homocysteinemia not only accelerates atherosclerosis but also by various mechanisms can increase the incidence of cerebrovascular disease.* ***MATERIAL & METHODS****: It was an observational (case control) study done from November 2017 to 2018. The present study was carried out on 50 patients (cases) admitted in the Medicine department, King George Hospital, Visakhapatnam. About 50 asymptomatic controls were taken. Demographic data like gender and age were collected, and the patients were interviewed. Investigations were done including fasting blood sugar, lipid profile, plasma Homocysteine levels. Homocysteine values more than 10 micromol/l were considered as Hyper homocysteinemia.* ***RESULTS****: Mean age among cases was 60.68 and among controls 63.44 years. The gender composition among cases were males 58%, females 42% and among controls males 60%, females 40%. Present study included age, sex, and BMI matched individuals. The percentage of hyper homocysteinemia (>10) among male is 57,9%, females is 42.1% & with normal homocysteine values (<10) in males 62.8%, females 37.2%. The mean homocysteine value among 50 cases is 19.44± 5.84, whereas, in controls, the mean values were 9.24 ± 1.93.* ***CONCLUSIONS****: The mean Homocysteine values in patients above the age of 45 years were significantly elevated than asymptomatic control. Hence Homocysteine should be assessed routinely in all patients with ischemic stroke*
Key Words*: Plasma homocysteine levels, ischemic stroke, case control study*

Date of Submission: 14-07-2021 Date of Acceptance: 30-07-2021

I. Introduction

Cerebrovascular disease designates any abnormality of the brain resulting from a pathologic process of the blood vessels. The pathologic process may result in ischaemic of the blood vessels resulting in infraction of the brain as spontaneous Hemorrhage into (or) around the brain.

Stroke of all types ranks third as a cause of death, and this is the leading cause of disability in adults. Ischaemic events account for approximately 80% of all strokes.[1]

MAGNITUDE OF THE PROBLEM;[1,2]

The incidence in the UK is approximately 2 per 1000 population per year, and about 100,000 patients have a first stroke every year, one every 5 minutes or so.

In the United States every year, there are approximately 500,000 cases of stroke, roughly 400,000 infractions, and 100,000 hemorrhages.

In India, based on a single population based study, the two year prevalence and annual incidence rate are 84 and 13 per 100,000 population, which, when compared with figures quoted from western studies, are much less.

HOSPITAL DATA[3,4,5]

Based on many retrospectives and a few prospective studies, cardiovascular disease accounts for 0.9% to 4.5% of total medical admissions in India. A few Indian studies point out that 9.2% to 30% of neurological admissions are patients suffering from a stroke.

The figures are much lower than the figures of Fisher et al. from the U.S.A. where about 50% of neurological admissions are patients with cerebrovascular diseases. As pointed out by Wad, if Indian figures were to be calculated only for adult Neurological hospital admissions excluding the pediatric age group, there might come closer to those mentioned by Fisher et.al. This contention, however, is not held by Venkataraman et al., who state that Cerebrovascular disease constitutes 18.8% of all admissions to the Neurological services of AIIMS.

Steep decreases in stroke incidence and mortality have occurred in the industrialized nation in recent years. Despite these trends in developed countries, stroke mortality and incidence are still high in many other countries. Socioeconomic factors, dietary and lifestyle behaviors, different patterns of risk factors, and environmental conditions may explain the different incidences of stroke observed in different parts of the world.

Several risk factors that may be classified as modifiable and unmodifiable increase the risk of ischaemic stroke. The modifiable risk factors have very much clinical significance because modification or alteration of these risk factors can decrease the incidence of stroke in the population. The modifiable risk factors of clinical significance are Hypertension, Diabetes mellitus, Dyslipidemia, Cigarette Smoking, Alchohol consumption, increased fibrinogen, elevated Homocysteine, obesity, etc.

Increased plasma levels Homocysteine is now considering as individual risk factors for cerebrovascular disease, myocardial infarction, and peripheral arterial occlusive disease. Hyperhomocysteinemia not only accelerates atherosclerosis but also by various mechanisms can increase the incidence of cerebrovascular disease.[6,7]

The present study is aimed to determine the plasma homocysteine levels in patients presenting with ischaemic stroke aged above 45 years and compare it with age and sex-matched controls.

II. Material & Methods

STUDY DESIGN: Observational study (case-control)

STUDY PERIOD: From November 2017-2018

The present study was carried out on 50 patients (cases) admitted in the Medicine department, King George Hospital, Visakhapatnam. About 50 asymptomatic controls were taken. The patients in this study satisfied the following inclusion criteria.

Inclusion criteria;

▪ All patients should be aged more than 45 years.

▪All patients first-ever diagnosed with having Ischaemic stroke were taken into the present study.

▪Patients who gave valid consent

Exclusion criteria:

Patients with

▪Ischaemic stroke of less than 45 years of age was excluded

▪Presenting with more than 48 hours of duration from the onset of ischaemic stroke were excluded

▪Patients who are on drugs that modify the result of homocysteine were excluded ….

Cholestyramine, Methotrexate, L-dopa, Niacin, Theophylline, Androgens, Cyclosporines, Fibric acid derivatives, Phenytoin, Carbamazepine.

▪Prior history of Renal failure, Hypothyroidism, SLE, Psoriasis excluded.

Data collection:

Demographic data like gender and age were collected, and the patients were interviewed for the relevant history such as diabetes mellitus, hypertension, heart disease, personal history, and family history. A thorough general physical examination was conducted, followed by a systemic examination, and the findings were noted. Height and weight for each participant were measured. BMI was expressed as weight in kilograms divided by square of height in meters(kg/m2)

Investigations;

▪ Fasting blood samples were drawn for following investigations

▪ Fasting blood sugar, Lipid profile (total cholesterol, triglycerides, HDL and LDL)

▪ Plasma Homocysteine levels.

▪ Homocysteine values more than 10 micromol/l were considered as Hyper homocysteinemia.

III. Results:

Mean age among cases was 60.68 and among controls 63.44 years. The gender composition among cases were males 58%, females 42% and among controls males 60%, females 40%. Mean BMI among cases and controls was 24.24 and 23.33 respectively. So the present study included age, sex, and BMI matched individuals.

Table No 1: Comparison of mean homocysteine levels between cases & controls

Homocysteine	N	Mean	Standard deviation	p-value
Cases	50	19.44	5.84	0.001
Controls	50	9.24	1.93	

The mean homocysteine value among 50 cases is 19.44± 5.84, whereas, in controls, the mean values were 9.24 ± 1.93, the P-value is < 0.001.
The percentage of hyper homocysteinemia (>10) among male is 57,9%, females is 42.1% & with normal homocysteine values (<10) in males 62.8%, females 37.2%.

Table No 2: Risk factor analysis among cases & controls

Risk factor	Cases N (%)	Controls N (%)
Hypertension	26 (52%)	41 (82%)
Diabetics	14 (28%)	13 (26%)
Smokers	16 (32%)	12 (24%)
Abnormal LDL	13 (26%)	7 (14%)

The mean homocysteine values among smokers was 19.39 and among non-smokers 19.47 and it was not significant statistically. The mean homocysteine values among diabetic was 19.39 and among non-diabetic 19.47 and it was not significant statistically. The mean homocysteine values among hypertensive was 19.95 and among non-smokers 18.97 and it was not significant statistically. The mean homocysteine values among patients with LDL >190 was 22.01 and among normal LDL patients 18.54 and it was not significant statistically.

Table No 3: Odd's Ratio

	Cases	Controls	Total
Homocysteine >10	45 (a)	12 (b)	69
Homocysteine <10	5 (c)	38 (d)	31
Total	50	50	100

P value= 0.001
Exposure rate among cases = a/a+c= 45/45+5=45/50=0.9
Exposure rate among controls = b/b+d= 12/12+38=12/50=0.24
Odd's ratio= ad/bc= (45×38) % (5×12)=28.5

The ODDs ratio gives the strength of the association between a risk factor and stroke. In the present study out of 50 patients 45 had homocysteine levels >10 µmol/L whereas 5 had homocysteine levels < 10 µmol/L and out of the 50 controls 12 had homocysteine levels >10 µmol/L, and 38 had homocysteine levels < 10 µmol/L with Odd's ratio being 28.5.

IV. Discussion

Stroke is universally affecting the entire human race. Stroke remains a major cause of mortality and morbidity worldwide. The burden of stroke arises largely from the elderly population. The present study has shown an elevation of Homocysteine levels > 10 µmol/L in 89% of patients aged above 45 years. Dr. Nigel Tan et al. had found an elevation of homocysteine > 10 µmol/L in 78% of patients of Ischemic stroke aged above 45 years.[8]

The mean homocysteine levels among the 50 patients in the present study were 19.44 ± 5.84 in contrast to controls who had a mean value of 9.24 ± 1.93. There is a significant difference between the patients and the controls. The p-value is < 0.001 that is statistically significant.

A similar study was conducted by Dr. Nigel Tan, Dr. N. Venkata Subramanian et al. in which they had selected 109 cases and 88 controls. The mean Homocysteine values in cases were 15.7, and that of in controls was 9.8, with a p-value of < 0.001. Hence plasma homocysteine levels are to be measured regularly among patients with Ischaemic stroke.[8]

The British regional heart study, the Rotterdam study of the elderly, and the Framingham studies, which were cohort studies, have shown elevated plasma homocysteine levels in Ischaemic strokes.

Study by Niazi F et al (2019) observed that the mean age of the 71 patients in the study was 35.8 years. Overall, 36 (50.7%) cases had hyper-homocysteinemia. The frequency was significantly higher in males

and in the age group 36-45 years (63.4%). Levels of homocysteine did not significantly affect the outcome at discharge.[9]

HOMOCYSTEINE AND SEX DISTRIBUTION

The present study has 29 male patients and 21 female patients. The p-value in the patient's group, when compared between males and females, was 0.68 indicating that there was no statistically significant difference between males and females.

Since the present study was conducted in patients above 45 years of age, most of the female patients might have been removed from the protective function of estrogens. So there was no statistical significance.

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.[10]

HOMOCYSTEINE AND HYPERTENSION :

In the present study number of patients having hypertension was 24 (48%). The mean and standard deviation of homocysteine levels in the hypertensive patient's group was 19.95 ± 6.10. The mean homocysteine levels of the non hypertensives The patient group was 18.97± 5.68 p-value is less than 0.055, which is statistically significant.

In the study conducted by Dr.Nigel Tan et al., the percentage of cases having diabetes was 28%, and the percentage of cases having diabetes was 28%, and the percentage of cases not having diabetes was 72%, and the p values were 0.001.[8]

HOMOCYSTEINE AND DYSLIPIDEMIA :

In the present study, the number of cases having dyslipidemia was 13, which is 26%, and the number of cases not having dyslipidemia was 37, which is 74%. The mean homocysteine levels of cases with dyslipidemia was 22.01 ± 6.52, and the mean homocysteine levels of the cases without dyslipidemia was 18.54 ± 5.39 The p-value was 0.05, so it is statistically significant.

In the study conducted by Dr.Nigel Tan et al. percentage of cases having dyslipidemia was 20%, and the percentage of cases not having dyslipidemia was 80%, and the p-value was < 0.001.[8]

HOMOCYSTEINE AND SMOKING:

In the present study number of cases who were current smokers was 16 that is 32%, and number cases who were non-smokers were 34 that is 68%. The mean homocysteine levels in non smokers were 19.47 ± 5.97, and that of the cases with a history of smoking was 19.39 ± 5.76 the p-value was 0.96,which is not significant.

Another similar kind of case control study by Gajbhare PT et al. (2017) found that total plasma fasting homocysteine level in case group was 30.10±14.8 µmol/L and control group was 13±5.3 µmol/L, (p=0.001). Elevated fasting homocysteine level was found in 76.66. 0% of ischemic stroke cases and in 10% of healthy controls (p=0.001). Serum homocysteine levels were higher in subjects having risk factors such as dyslipidemia (p value <0.001), active lifestyle (p value <0.05) and smoking (p value<0.05). Serum homocysteine did not show any significant relation with age, sex, diabetes mellitus, diet pattern and defective coagulation (p value >1).[11]

V. **Conclusions**:

The mean Homocysteine values in patients above the age of 45 years were significantly elevated than asymptomatic control. Hence Homocysteine should be assessed routinely in all patients with ischemic stroke. The present study addresses the fact that hypertension, diabetes mellitus, dyslipidemia, and smoking are important risk factors for ischemic stroke. The mean homocysteine levels were more in patients with risk factor group than in the non-risk factor group. This infers that patients with risk factors should be assessed for homocysteine levels and homocysteine is a predominant independent risk factor for ischaemic stroke.

References:

[1]. Kim AS, Johnston SC.Global variation in the relative burden of stroke and ischemic heart disease.Circulation. 2011; 124:314–323.

[2]. Pniewski J, Chodakowska-Zebrowska M, Woźniak R, Stepień K, Stafiej A. Plasma homocysteine level and the course of ischemic stroke. Acta Neurobiol Exp (Wars). 2003;63(2):127-30. PMID: 12926539.

[3]. Boysen G, Brander T, Christensen H, Gideon R, Truelsen T. Homocysteine and risk of recurrent stroke. Stroke. 2003;34(5):1258-61.

[4]. Perry IJ. Homocysteine, hypertension and stroke. J Human Hypertens. 1999;13:289-93.

[5]. Pinto A. Cerebrovascular risk factors and clinical classification of strokes. Semin Vasc Med. AUG;4(3):287-303.

[6]. Brattstrom LE, Hardebo JE, Hultberg BL. Moderate homocysteinemia: a possible risk factor for arteriosclerotic cerebrovascular disease. Stroke. 1984;15:1012-6.

[7]. Narang, APS, Verma I, Kaur S, Narang A, GuptaS, Avasthi G. Homocysteine- Risk factor for ischemic stroke?. Indian J Physiol Pharmacol. 2009;53(1):34-8.

[8]. Tan NC, Venketasubramanian N, Saw SM, Tjia HT. Hyperhomocyst (e) inemia and risk of ischemic stroke among young Asian adults. Stroke. 2002;33(8):1956-62.

[9]. Niazi F, Aslam A, Khattak S, Waheed S. Frequency of Homocysteinemia in Young Ischemic Stroke Patients and Its Relationship with the Early Outcome of a Stroke. Cureus. 2019;11(9):e5625.
[10]. Kang SS, Wong PWK, Cook HY et al. Protein-bound homocysteine: A possible risk factor for coronary artery disease. J Clin Invest. 1986;77:1482-6.
[11]. Gajbhare PT, Juwale NI. The study of plasma homocysteine level as a risk factor for ischemic strokes in young patients Int J Adv Med 2017;4:1019-25.

: Dr.K.Srinivas, et. al. "A Study of Plasma Homocysteine Levels In Ischaemic Stroke." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(07), 2021, pp. 51-55