ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Original Research Article

A Cross Sectional Study on Clinical Profile and Risk Factors of Stroke with Special Emphasis on Homocysteine Levels

Dr. Ranjith V.[1], Dr, Srinivas K.[2], Dr. Dinesh P.V.[3]

[1]Assistant Professor, Department of General Medicine, Mysore Medical College, Mysore, Karnataka, India.

[2]Assistant Professor, Department of General Medicine, Mysore Medical College, Mysore, Karnataka, India.

[3]Professor & HOD, Department of Community Medicine, KVG Medical College, Sullia, Karnataka, India.

Corresponding Author

Dr. Dinesh P. V., Professor & HOD, Department of Community Medicine, KVG Medical College, Sullia, Karnataka, India.

Received: 11-12-2023 / Revised: 16-12-2023 / Accepted: 14-01-2024

ABSTRACT

BACKGROUND

Stroke is one of the leading causes of death and disability. It is now becoming an important cause of premature death and disability in a country like India. There are many risk factors for stroke which include age, smoking, alcohol consumption, physical inactivity, hypertension, dyslipedemia, diabetes mellitus, obesity, cardiovascular diseases and metabolic syndrome. Certain biochemical factors have also been implicated as a definite modifiable risk factor.

OBJECTIVE

To describe the clinical profile of patients admitted with stroke and also to identify the risk factors of stroke with special emphasis on homocysteine levels.

MATERIALS AND METHODS

A cross sectional study was conducted among 100 stroke patients admitted at a tertiary care teaching hospital in Mysore between April 2017 to March 2020. Permission from Institutional Ethics Committee was obtained before the start of the study. Blood was obtained from all patients and the results obtained were entered in the preformed performa along with other clinical parameters.

RESULTS

Most of the patients (41%) belonged to the age group of 60 to 79 years and were males (84%). 94% had infarct and 6% had cerebral haemorrhage. Proportion of patients who had hypertension, diabetes, were smokers, and consumed alcohol were 46%, 22%, 50% and 61% respectively. The mean serum homocysteine level was 18.19 ± 9.98. Serum cholesterol and serum homocysteine were significantly higher in the younger age group when compared to those in age group of more

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

than 45 years. Patients without diabetes had high homocysteine levels when compared to diabetic patients. A negative relationship between age and homocysteine levels was seen.

CONCLUSION

The incidence of stroke was highest in males belonging to the age group of 60 to 79 years with hemiplegia being the most common presentation and middle cerebral artery being the most common vascular territory involved. Higher serum triglycerides and homocysteine levels were significantly associated with young stroke. A negative correlation between diabetes, age and homocysteine levels was seen.

KEY WORDS

Risk factors, Stroke, Serum Homocysteine levels

INTRODUCTION

Worldwide, cerebrovascular accidents (stroke) are the second leading cause of death and the third leading cause of disability.[1] It is a major global public health problem. World Health Organization (WHO) defines stroke as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin.[2] Stroke may either be secondary to ischemia or hemorrhagic disturbances of the cerebral blood circulation.

Globally, 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years occur in low- and middle-income countries.[3-5] Over the last four decades, the stroke incidence in low- and middle-income countries has more than doubled. During these decades stroke incidence has declined by 42% in high-income countries.[3]

Risk factors for stroke include age, smoking, alcohol consumption, physical inactivity, hypertension, dyslipedemia, diabetes mellitus, obesity, cardiovascular diseases, metabolic syndrome, history of cerebrovascular event and genetic risk factors.[6,7,8] Elevated levels of homocysteine is considered as a definite modifiable risk factor for ischaemic stroke[9,10,11,12] and recently for haemorrhagic stroke as well.[13]

Homocysteine is an intermediate in the methionine metabolism and can cause vascular injury and atherosclerotic plaque instability.[14] Hyperhomocysteinemia is defined as an elevated levels of total homocysteine concentration (>10 μM/l) in plasma.[15] As compared to concentrations below 9μM/l, there is nine-fold increase in the risk of myocardial infarction and stroke with total plasma homocysteine levels above 20 μM/l.[16]

The objective of the present study is to describe the clinical profile of patients admitted with stroke and also to identify the risk factors of stroke with special emphasis on homocysteine levels.

Materials and Methods

A cross sectional study was conducted among 100 stroke patients admitted at a tertiary care teaching hospital in Mysore between April 2017 to March 2020. Diagnosis of stroke was based on history of the patient, clinical features, CT scan of brain and MRI if needed. All the patients were subjected to the following blood investigations: Complete blood count, Random blood sugar, Serum cholesterol, Serum triglyceride, Blood urea, Serum creatinine, fasting serum homocysteine level, ECG, Fundoscopy, Carotid Doppler and Echocardiogram.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Study commenced only after approval of the study protocol by Institutional Ethics Committee. All the patients (caregivers of comatose patients) were explained the nature of study and a written informed consent was taken before the study.

4 ml blood was collected in EDTA coated tubes. The serum was separated by centrifugation. Serum homocysteine was measured by fluorescein polarization immunoassay (FPIA).

Operational Definition

Waist Hip Ratio: The cut off values for waist hip ratio (WHR) were 0.89 for men and 0.81 for women.[17]

Hypertension: Previously receiving antihypertensive medication or when the patient was previously diagnosed with hypertension or detecting blood pressure of ≥ 140/90 mm/Hg for two measurements.[18,19]

Diabetes Mellitus: If the patient was previously on oral hypoglycemic agents/insulin treatment or had the diagnosis of any type of DM or FBS ≥ 126 mg/dl or had a documented RBS ≥ 200 mg/dl or glycosylated hemoglobin of ≥6.5%.[18,19]

Alcohol Abuse/ Consumption: on average ≥ 2 drinks/day for males and ≥ 1 drinks for females (previous drinker: ex drinker for more than 1 year).[20]

Smoker: On average 2 cigarettes per day in men and 1 per day in women [21]

- Former smoker: who abstained from smoking for greater than 1 years.[22]
- Current smoker: smoking within 1 year ago.[22]

RESULTS

Sl. No.	Variables	No. of Patients
Age Distribution	20 – 29 Years	3 (3%)
	30 – 39 Years	13 (13%)
	40 – 49 Years	19 (19%)
	50 – 59 Years	16 (16%)
	60 – 69 Years	21 (21%)
	70 – 79 Years	20 (20%)
	80 – 89 Years	6 (6%)
	90 – 99 Years	2 (2%)
Sex Distribution	Male	84 (84%)
	Female	16 (16%)
Waist Hip Ratio	Normal	39 (39%)
	Increased	61 (61%)
History of Hypertension	Present	46 (46%)
	Absent	54 (54%)
History of Diabetes	Present	22 (22%)
	Absent	78 (78%)
History of Smoking	Present	50 (50%)
	Absent	50 (50%)
History of Alcohol Consumption	Present	61 (61%)
	Absent	39 (39%)
Type of Stroke	Infarct	94 (94%)
	Haemorrhage	6 (6%)

Table 1: Baseline Characteristics of the Patient

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Sl. No.	Laboratory Parameters	Less than 45 Years (31)	More than 45 Years (69)	T Value	P Value
1	Haemoglobin	10.81 ± 4.46	12.71 ± 3.41	2.3354	0.0216*
2	Random Blood Sugar	160 ± 87.16	149.98 ± 64.23	0.6434	0.5215
3	Serum Creatinine	1.7 ± 2.87	1.06 ± 0.43	1.8184	0.0721
4	Total Cholesterol	151.45 ± 41.04	171.58 ± 52.40	1.8922	0.0614
5	Serum Triglycerides	214.81 ± 224.20	143.73 ± 55.94	2.4809	0.0148*
6	Serum Homocysteine	22.18 ± 7.83	16.39 ± 10.36	2.7732	0.0066*

Table 2: Laboratory Parameters Stratified Based on Age

Sl. No.	Laboratory Parameters	Male (84)	Female (16)	T Value	P Value
1	Haemoglobin	12.55 ± 3.86	10.84 ± 3.18	1.6656	0.0990
2	Random Blood Sugar	155.07 ± 74.39	142 ± 54.64	0.6681	0.5056
3	Serum Creatinine	1.30 ± 1.66	0.85 ± 0.11	1.0795	0.2830
4	Total Cholesterol	157.63 ± 47.74	215.71 ± 33.03	4.6494	<0.0001*
5	Serum Triglycerides	165.5 ± 110.74	105.85 ± 23.87	2.1368	<0.0351*
6	Serum Homocysteine	17.87 ± 10.76	19.86 ± 3.62	0.7293	0.4675

Table 3: Laboratory Parameters Stratified Based on Gender

Sl. No.	Type of Stroke	Serum Homocysteine Levels	T Value	P Value
1	Infarct (94)	18.24 ± 9.90	0.2110	0.8333
2	Haemorrhage (6)	19.13 ± 12.01		

Table 4: Serum Homocysteine Levels in Infarct and Haemorrhagic Stroke

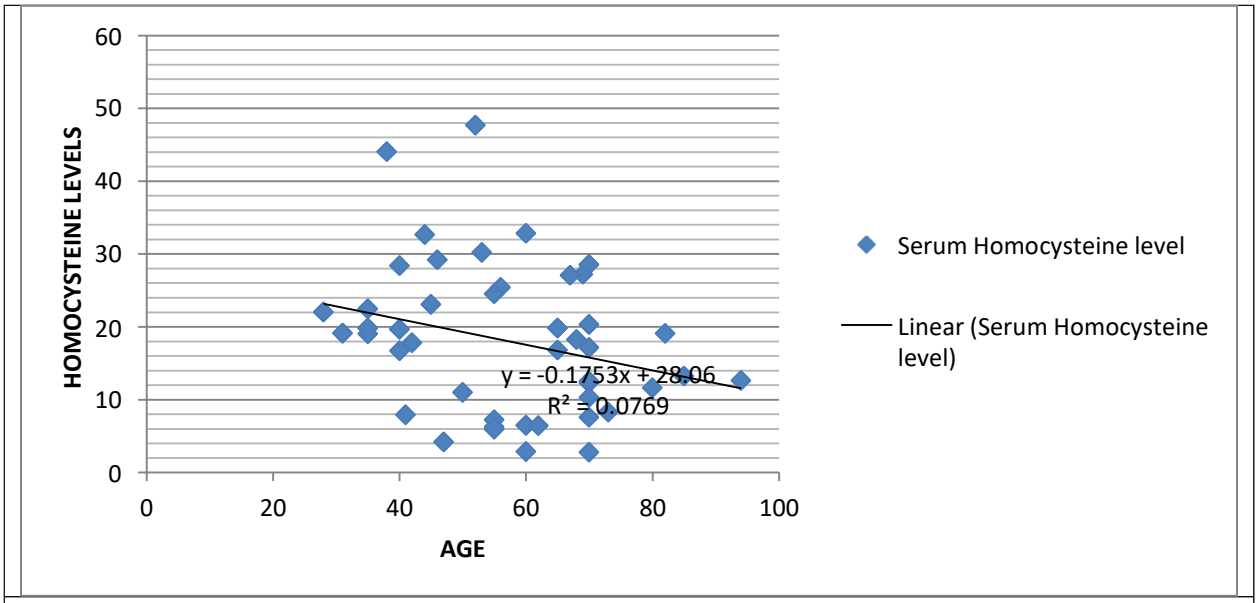

Figure 1: Correlation between Age and Homocysteine Levels

The study was conducted among 100 stroke patients admitted in a tertiary care teaching hospital. Most of the patients (41%) belonged to the age group of 60 to 79 years and were males

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

(84%). The mean age of the stroke patients was 56.3 ± 15.79. 61% of the patients were obese on the basis of the waist hip ratio. 46% of the patients presented with a history of hypertension and 22% gave a history of diabetes. The proportion of patients who smoked tobacco and consumed alcohol were 50% and 61% respectively. Maximum number of patients (94%) admitted had an infarct and the rest of them (6%) had haemorrhage (Table 1).

The mean levels of haemoglobin, random blood sugar, serum creatinine, total cholesterol and serum triglycerides were 12.20 ± 3.78, 152.97 ± 71.47, 1.23 ± 1.55, 166.66 ± 50.19 and 159.69 ± 117.40 respectively. The mean serum homocysteine level was 18.19 ± 9.98. The laboratory parameters were stratified based on the age. Serum cholesterol and serum homocysteine were significantly higher in the younger age group when compared to those in age group of more than 45 years. There was significant difference in total serum cholesterol and triglyceride levels between males and females. The serum homocysteine levels however showed no significant difference between the genders. There was no significant difference in serum homocysteine levels between patients with infarct and haemorrhagic stroke.

A chisquare test was applied to see if there was a relationship between hypertension, diabetes mellitus, alcohol intake and smoking with presence of homocysteinemia. It was seen that patients without diabetes had high homocysteine levels when compared to diabetic patients and this relationship was statistically significant.

A Pearson correlation was done to check the relationship between age, total cholesterol and serum triglycerides with homocysteine levels. It was found that there was a negative relationship between age and homocysteine levels and this was statistically significant.

DISCUSSION

The study was conducted among 100 patients who had stroke and were admitted in a tertiary care teaching hospital. The mean age of the study population was 56.3. This finding was similar to other studies.[23,24,25] It is believed that the average age of patients with stroke in developing countries is 15 years younger than that in developed countries.[26,27] In India, nearly one-fifth of patients with first ever strokes admitted to hospitals are aged 40 years.[28] The proportion of females in this study was 16% which is lower than that seen in other studies.[23,24,25] The mean age and gender distribution was slightly lower than that of Western and Chinese population.[23,24,25] Almost 51% of the patients belonged to less than 60 years age group which reflects the financial burden because of stroke in India. The higher proportion of males indicates that there still exists some cultural barriers which prevents women from seeking medical care.

It has been estimated that hypertension causes 54% of stroke mortality in low-income and middle-income countries, followed by high cholesterol (15%) and tobacco smoking (12%).[29] It was observed in the present study that atleast 50% of the patients either smoked or consumed alcohol or both. Of those who were found to use tobacco in some form, 76% smoked cigarattes. The limitation of this study is that the investigators enquired only about current smoking and probably this could have underestimated the risk factor. It was found in a study that, young stroke subjects were 8 times more likely to have had smoked tobacco.[30]

Several studies have reported that homocysteinemia is associated with two to threefold increased risk of ischemic stroke.[31,32,33,34] Several factors contribute to increased plasma homocysteine levels. Individuals with pre-existing atherosclerosis have higher homocysteine levels than those without pre-existing atherosclerosis. Higher prevalence of homocysteinemia in

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

many developing countries could indicate the role of inadequate intake of vitamins and antioxidants in the multi-factorial causes of stroke.[31,35]

In the present study, the homocysteine levels were negatively associated with age. In a study conducted by Lakshmikumar K et al.[36] it was seen that serum homocysteine levels increases with age from 20 to 49 years. However, in the 50 -60 years age group, there was decline in homocysteine levels. The findings in the present study and that of Lakshmikumar K et al are different from other studies.[37,38]

In the present study, euglycemic patients had a higher homocysteine level when compared to diabetic patients. This finding was similar to that seen in a study conducted by Daniel E Platt[39] where a significant negative correlation was observed between homocysteine levels and type II diabetes mellitus.

CONCLUSION

The incidence of stroke was highest in males belonging to the age group of 60 to 79 years. Hemiplegia was the most commonest mode of presentation and middle cerebral artery was the most common vascular territory involved. Although hypertension, diabetes mellitus, smoking, alcohol consumption and obesity are considered as risk factors for stroke, higher serum triglycerides and homocysteine levels were significantly associated with young stroke. There was a negative correlation between diabetes, age and homocysteine levels.

REFERENCES

[1] Global Health Estimates. Geneva: World Health Organization; 2012. Available from: http://www.who.int/healthinfo/global_burden_disease/en/. Accessed on 12th May 2019.
[2] WHO MONICA Project Investigators. The World Health Organization MONICA Project (Monitoring trends and determinants in cardiovascular disease). J Clin Epidemiol 1988;41:105-114.
[3] Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group. Global and regional burden of stroke during 1990-2010: Findings from the Global Burden of Disease Study 2010. Lancet 2014;383(9913):245–54.
[4] Feigin VL, Lawes CMM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 2009;8(4):355-69.
[5] Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007;6(2):182-7.
[6] Bang OY, Ovbiagele B, Kim JS. Nontraditional risk factors for ischemic stroke: An update. Stroke 2015;46(12)3571-8.
[7] von Sarnowski B, Putaala J, Grittner U. Lifestyle risk factors for ischemic stroke and transient ischemic attack in young adults in the stroke in young fabry patients study. Stroke 2013;44(1):119-25,
[8] Hankey GJ, Eikelboom JW. Homocysteine and stroke. Current Opinion in Neurology 2001;14:95-102.
[9] Li Z, Li S, Hongye Z, Yuhua L, Daowen W. Elevated plasma homocysteine was associated with haemorrhagic and ischaemic stroke, but methylenetetrahydrofolate reductase gene C677T polymorphism was a risk factor for thrombotic stroke. A multi centre case-control study. Stroke 2003;34:2085–90.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

[10] Tascilar N, Ekem S, Aciman E, Ankarali H, Mungan G, Ozen B, et al. Hyperhomocysteinemia as an independant risk factor for cardioembolic stroke in Turkish population. Tohoku J Exp Med 2009;218(4):293-300.
[11] Manolescu BN, Oprea E, Farcasanu IC, Berteanu M, Cercasov C. Homocysteine and vitamin therapy in stroke pre vention and treatment: a review. Acta Biochimica Polonica 2010;57(4): 467-7.
[12] Murmu M, Karun MKP, Dash S, Singh LK, Kar A, Mishra P. Study of serum homocysteine level in cases of non-diabetic ischemic stroke. Int J Res Med Sci 2018;6(5):1611-6.
[13] Li Z, Li S, Hongye Z, Yuhua L, Daowen W, et al. Elevated plasma homocysteine was associated with haemorrhagic and ischaemic stroke, but methylenetetrahydrofolate reductase gene C677T polymorphism was a risk factor for thrombotic stroke. A multi centre case-control study. Stroke 2003;34:2085-90.
[14] Fu Y, Wang X, Kong W. Hyperhomocystenemia and vascular injury: advances in mechanisms and drug targets. Br J Pharmacol 2018;175(8):1173-89.
[15] Manolescu BN, Oprea E, Farcasanu IC, Berteanu M, Cercasov C. Homocysteine and vitamin therapy in stroke pre vention and treatment: a review. Acta Biochimica Polonica 2010;57(4): 467-7.
[16] Murmu M, Karun MKP, Dash S, Singh LK, Kar A, Mishra P. Study of serum homocysteine level in cases of non-diabetic ischemic stroke. Int J Res Med Sci. 2018;6(5):1611-6.
[17] Snehalatha C, Viswanathan V, Ramachandran A. Cut off values for normal anthropometric variables in Asian Indian adults. Diabetes Care 2003;26(5):1380-84.
[18] Manorenj S, Inturi S, Jyotsna B, Sai Savya V, Areli D, Balarami Reddy O. Prevalence, pattern, risk factors and outcome of stroke in women: a clinical study of 100 cases from a tertiary care center in South India. Int J Res Med Sci 2016;4(6):2388-93.
[19] Deresse B, Shaweno D. Epidemiology and in-hospital outcome of stroke in South Ethiopia. J Neurol Sci 2015;355(1–2):138–42.
[20] Wu CY, Wu HM, Lee JD, Weng HH. Stroke risk factors and subtypes in different age groups: a hospital-based study. Neurol India 2010;58(6):863-8.
[21] Fekadu G, Chelkeba L, Kebede A. Risk factors, clinical presentations and predictors of stroke among adult patients admitted to stroke unit of Jimma university medical center, south west Ethiopia: prospective observational study. BMC Neurology 2019;19:187.
[22] Gezmu T, Schneider D, Demissie K, Lin Y, Gizzi MS. Risk factors for acute stroke among south Asians compared to other racial/ethnic groups. PLoS One 2014;9(9):e108901.
[23] Schneider AT, Kissela B, Woo D, Kleindorfer D, Alwell K, Miller R, et al. Ischemic stroke subtypes: a population-based study of incidence rates among blacks and whites. Stroke 2004;35:1552-6.
[24] Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 2009;8:355-69.
[25] Tsai CF, Thomas B, Sudlow CL. Epidemiology of stroke and its subtypes in Chinese vs white populations: a systematic review. Neurology 2013;81:264-72.
[26] Bonita R, Mendis S, Truelsen T, Bogousslavsky J, Toole J, Yatsu F. The global stroke initiative. Lancet Neurol 2004;3:391-3.
[27] Poungvarin N. Stroke in the developing world. Stroke 1998;352:19-22.
[28] Pandian JD, Padma V, Vijaya P, Sylaja PN, Murthy JMK. Stroke and thrombolysis in developing countries. Int J Stroke 2007;2:17–26.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

[29] Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007;6:182-7.
[30] Lipska K, Sylaja PN, Sarma PS, Thankappan KR, Kutty VR, Vasan RS, Radhakrishnan K. Risk factors for acute ischaemic stroke in young adults in South India. J Neurol Neurosurg Psychiatry 2007;78:959-63.
[31] Christopher R, Nagaraja D, Shankar SK. Homocysteine and cerebral stroke in developing countries. Curr Med Chem 2007;14:2393-401.
[32] Tan NC, Venketasubramanian N, Saw SM, Tjia HT. Hyperhomocyst(e)inemia and risk of ischemic stroke among young Asian adults. Stroke 2002;33:1956-62.
[33] Fallon UB, Virtamo J, Young I, McMaster D, Ben-Shlomo Y, Wood N, et al. Homocysteine and cerebral infarction in finnish male smokers. Stroke 2003;34:1359-63.
[34] Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease Probable benefits of increasing folic acid intakes. JAMA 1995;274:1049-57.
[35] Sánchez-Moreno C, Jiménez-Escrig A, Martín A. Stroke: roles of B vitamins, homocysteine and antioxidants. Nutr Res Rev 2009;22:49-67.
[36] Lakshmikumar K, Gomti K, Shugeta ND, Arbind RS. Effect of age on homocysteine level among adult urban population of Manipur. J Med Soc 2013;27:46-8.
[37] Ganji V, Kafai MR. Demographic, lifestyle, and health characteristics and serum B vitamin status are determinants of plasma total homocysteine concentration in the post-folic acid fortification period, 1999-2004. J Nutr 2009;139:345-52.
[38] Saw SM, Yuan JM, Ong CN, Arakawa K, Lee HP, Coetzee GA, et al. Genetic, dietary, and other lifestyle determinants of plasma homocysteine concentrations in middle-aged and older Chinese men and women in Singapore. Am J Clin Nutr 2001;73:232-9.
[39] Platt DE, Hariri E, Salameh P, Merhi M, Sabbah N, Helou M, et al. Type II diabetes mellitus and hyperhomocysteinemia: a complex interaction. Diabetol Metab Syndr 2017;9:19.