Original Article

Elevated Homocysteine Levels in Patients with Acute Ischemic Stroke

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ABSTRACT

Objective: To determine the plasma homocysteine levels in patients with acute ischemic stroke at a tertiary care Hospital, Karachi.

Study Design: A Cross Sectional study.

Place and Duration of Study: This study was conducted at the Department of General Medicine, Liaquat National Hospital, Karachi from October 2019 to April 2020.

Materials and Methods: All patients who fulfilled the inclusion criteria in the Department of General Medicine Liaquat National Hospital & Medical College, Karachi were included. After taking informed written consent history was taken, clinical examination was done and blood sample was sent for serum homocystein level to assess the outcome i.e. frequency of hyperhomocysteinemia.

Results: Total of 191 patients of hyperhomocysteinemia with ischemic stroke was included. 120 patients (62.8%) were males & 71 patients (37.2%) were females with the mean age (years) was 51.2±11.4 years. Hyperhomocysteinemia was seen in 86(45%) patients.

Conclusion: In conclusion hyperhomocysteinaemia, a modifiable risk factor for ischaemic stroke, was seen in about half of ischemic stroke patients, was predominant in male gender and common in patients with advance age.

Key Words: Homocysteinemia, ischemic stroke, risk factors.

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INTRODUCTION

Stroke is among the leading causes of mortality and disability in both developed and developing countries.[1] Stroke (including ischaemic stroke and haemorrhagic stroke) affects 13.7 million people globally per year and is the second leading cause of death, with 5.5 million deaths per year.[2] Previous studies have shown a higher prevalence and higher in-hospital mortality compared with western countries.[3,4]

Homocysteine is a sulphur-containing amino acid derived from the metabolic demethylation of dietary methionine. A normal level of homocysteine in blood is 5-12mmol/L. High levels of homocysteine cause oxidative damage to vascular endothelium with proliferation of vascular smooth muscle and creates a prothrombotic environment through its action on platelets, thrombin and fibrin.[5] Many studies have shown an association between increased homocysteine level and a risk for atherosclerotic vascular disease.[6] Similarly studies have also reported a relationship between homocysteine levels and stroke.[7] Moreover, stroke patients with hyper-homocysteinaemia have more frequently developed cerebral microangiopathy and multiple infarctions compared to patients with normal homocysteine serum level.[8] Epidemiological research has shown that increased total homocysteine (tHcy) levels are associated with an increased risk of thromboembolic disease; however, controversy still exists over which subtype of stroke is allied to hyperhomocysteinemia.[9]

Elevated fasting homocystein level was found in 75.0% of ischemic stroke patient and in 16.67% of healthy controls (p=0.001).[10] Elevated fasting homocysteine level was found in 76.66% of ischemic stroke cases and in 10% of healthy controls.[11] Overall, 56 (58.3%) cases had hyper-homocysteinemia.[12]

This study will evaluate the frequency of homocysteinemia in patients with ischemic stroke. Several studies have shown homocysteinemia in patients with ischemic stroke.[10,12] However, the evidence is still lacking in a Pakistani population. The early suspicion is made to avoid diagnostic delay and to do further research to identify risk factors so that they can be avoided in our population. The objective of this

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study was to determine the plasma homocysteine levels in patients with acute ischemic stroke at a tertiary care Hospital, Karachi.

MATERIALS AND METHODS

A Cross Sectional Study was conducted in Department of General Medicine, Liaquat National Hospital, Karachi during October 2019 to April 2020. Ethical approval was obtained from Institutional Review Board Liaquat National Hospital, Karachi. A total 191 patients with ischemic stroke were required according to the sample size calculated by Raosoft calculator assuming frequency of homocysteinemia in patients with ischemic stroke 58.3% [1], confidence level 95%, and bond on error 7%.

Patients between 30 years to 70 years of age, either gender, with diagnosis of ischemic stroke as per operational definition for > 6 months and signed informed consent were selected through non-probability consecutive sampling technique. Patients not given informed consent, renal insufficiency (either known creatinine clearance < 30 ml/min/1.73m² or current medical care for severe renal insufficiency) and hemorrhagic stroke (CT scan showing hyperdense area) were excluded.

Subjects attending inpatient or outpatient department of General Medicine, Liaquat National Hospital, Karachi who was diagnosed case of ischemic stroke for > 6 months as per operational definition. In all these patients serum sample was taken and sent for homocysteine level to the institutional laboratory. Serum homocysteine levels >15µmol/L are diagnostic of hyperhomocysteinemia. All demography, clinical history was recorded by a principal investigator on a predesigned performa, informed written consent was taken before enrolment. Exclusion criteria were followed strictly to avoid confounding variables.

SPSS version 22 was used for data analysis. Frequencies and percentages were computed for categorical variables like gender, co-morbid conditions i-e DM, hypertension (yes/no), hyperhomocysteinemia (yes/no). Values were presented as mean ± standard deviation for continuous variables like age, duration of ischemic stroke, homocysteine level. Effect modifier like age, gender, duration of ischemic stroke, co-morbid conditions i-e DM, hypertension was controlled through stratification. Chi-square test was used. P ≤0.05 was considered level of significance.

RESULTS

A total of 191 patients of hyperhomocysteinemia with ischemic stroke selected to conduct this study. The mean age (years) was 51.2 ±11.4 years. A total of 120 patients (62.8%) were males & 71 patients (37.2%) were females. The mean duration of ischemic stroke (months) was 12.9 ±4.2 months. The mean Serum homocysteine level (mg/dl) was 20.5 ±13(Table I).

In our study diabetic mellitus was seen in 86(45%) patients and hypertension was seen in 58(30.4%) patients. In our study Hyperhomocysteinemia was seen in 86(45%) patients, as shown in Table-1. The frequencies of age (years) groups, gender, duration of ischemic stroke (months), diabetic mellitus & hypertension were calculated according to Hyperhomocysteinemia (Table II).

In our study Hyperhomocysteinemia was significantly associated with gender but not significantly associated with age, duration of ischemic stroke (months), diabetic mellitus & hypertension, with P-value of 0.098,0. 034, 0.454, 0.935, & 0.504 respectively.

Table No.1: (Descriptive statistics of Age, Duration of Ischemic stroke and Serum homocysteine level

Statistics	Age (Years)	Duration of Ischemic stroke (months)	Serum homocysteine level mg/dl
Minimum	30	6	5
Maximum	70	22	50
Mean	51.2	12.9	20.5
Std. Deviation	11.4	4.2	13

Table No.2: Hyperhomocysteinemia according to age, gender, duration of Ischemic stroke, diabetes mellitus and hypertension (n=191)

Age (years)	Hyperhomocysteinemia		P-value
	Yes	No	
30-50 years	42(22%)	55(28.6%)	0.098
51-70 years	44(23%)	50(26.4%)	
Male	47(24.6%)	73(28.2%)	0.034
Female	39(20.4%)	32(16.8%)	
Duration of Ischemic stroke (months) 6-14	53(28%)	71(37.2%)	0.454
15-22	33(17%)	34(17.8%)	
Diabetic mellitus Yes	39(20.4%)	47(24.6%)	0.935
No	47(24.6%)	58(30.4%)	
Hypertension Yes	24(12.6%)	34(17.8%)	0.504
No	62(32.5%)	71(37.2%)	

Chi-square test was applied. P-value ≤ 0.05 considered as significant.

DISCUSSION

Over the last decade, convincing evidence has been gathered on the relation between moderate elevation of plasma Hcy and ischemic stroke. Several studies have reported that HHcy is associated with two to threefold

increased risk of ischemic stroke.[13-15] A meta-analysis of 27 observational studies on Hcy and atherosclerotic vascular disease, of which 11 studies addressed the association between Hcy and risk of stroke. Nine case-control studies provided support for the hypothesis that Hcy is an independent risk factor for stroke, while 2 prospective studies reported negative results.[15]

The study showed a strong association between hyperhomocysteinemia and ischaemic stroke. In our study hyperhomocysteinemia was seen in 86(45%) patients as compare to Niazi et al[16] study in which the half of ischaemic stroke patients had hyperhomocysteinemia. This frequency is similar to the findings presented in some other studies. One study showed that hyperhomocysteinemia was found in 48% of ischaemic stroke patients. [17]

In another study, hyperhomocysteinemia was found in 50% of stroke patients, and stroke patients with hyperhomocysteinemia were found to have multiple infarctions and cerebral microangiopathy as compared to patients with normal serum homocysteine level.[18] Elevated fasting homocystein level was found in 75.0% of ischemic stroke patient and in 16.67% of healthy controls.[19] Elevated fasting homocysteine level was found in 76.66% of ischemic stroke cases and in 10% of healthy controls.[20] Overall, 56 (58.3%) cases had hyper-homocysteinemia.[21]

Major modifiable risk factors were similar to stroke patients elsewhere in the world. The most common risk factors in our stroke patients were diabetes mellitus and hypertension. Syed et al. reported that approximately 77% of their cohort had diabetes mellitus, hypertension, or both. [22] Hypertension was the commonest risk factor in our patients (38%) of the patients. Some studies have reported a relationship between hypertension and homocysteine levels.[23] In Niazi et al[16] study, the association was not statistically significant. Some other studies have also failed to establish any relation.[24] This further re-emphasizes the need for more research studies to observe the association between homocysteine levels and the traditional risk factors of stroke such as diabetes and hypertension.

In our study, hyperhomocysteinemia was predominant in in male gender which is similar to Niazi et al[16] study males had higher homocysteine levels than females. Another study also reported that males were found to have higher homocysteine levels than females.[25] In our study hyperhomocysteinemia was common in age group of 51-70 years as compare to Niazi et al[16] study also found that males in the age group of 36-45 years were especially found to be high homocysteine levels. Forty-five out of 71 (63%) patients were in the age group 36-45 years, 27 out of 45 (60%) had high homocysteine levels in Niazi et al[16] study. In an Indian study, the difference in homocysteine levels between males and females were statistically insignificant.[23]

The limitation of our study was single center study, smaller sample size. Further studies with larger sample sizes are required.

CONCLUSION

In conclusion hyperhomocysteinaemia, a modifiable risk factor for ischaemic stroke, was seen in about half of ischemic stroke patients, was predominant in male gender and common in patients with advance age.

Author's Contribution:

Concept & Design of Study:	Kamal Ahmed
Drafting:	Doniya Bahar, Muhammad Athar Khan, Wania Abbas
Data Analysis:	Abdul Aziz, Aisha
Revisiting Critically:	Kamal Ahmed, Doniya Bahar
Final Approval of version:	Kamal Ahmed

Conflict of Interest: The study has no conflict of interest to declare by any author.

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