

Frequency of hyper-homocysteinaemia in ischaemic stroke patients of Karachi

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Abstract

Objective: To find out the frequency of hyper-homocysteinaemia in ischaemic stroke patients and its relation with other risk factors.

Methods: The cross-sectional study based on convenience sampling was conducted at the Civil Hospital, Karachi, from May to July 2012. It comprised ischaemic stroke patients selected from the Out Patient Department and Emergency Department. An overnight 8-hour fasting venous blood sample (4ml in ethylenediaminetetraacetate) was drawn for analysis. Rest of the data was collected through a structured proforma and was analysed using SPSS 17.0.

Results: The mean age of the 96 patients in the study was 64.9±10.9 years (range: 40-85). Overall, 56(58.3%) cases had hyper-homocysteinemia. The frequency was significantly high in the age 60-79 age group ($p<0.007$).

Conclusion: Hyper-homocysteinaemia, a modifiable risk factor, is associated with a high number of ischaemic stroke patients. Hence, steps should be taken to minimise this risk factor by screening and early intervention.

Keywords: Hyper-homocysteinemia, Ischemic stroke, Frequency. (JPMA 64: 1063; 2014)

Introduction

Stroke is one of the main causes of mortality around the globe.¹ Every year, 15 million people in the world suffer a stroke, out of which 5 million people die and 5 million get disabled which creates a burden on the family and society.² Ischaemic stroke is a major problem in healthcare and it causes more morbidity than mortality. Hence, it is considered one of the most debilitating neurological disorders which imposes exorbitant expenses on the society.

Some risk factors for stroke are unchangeable such as age, gender and positive family history, while other risk factors can be modified such as hypertension, diabetes, hyperlipidaemia and hyper-homocysteinaemia. It has been reported that 70% of strokes are attributable to known risk factors.³ The best method to reduce the burden of stroke is efficient prevention of stroke. Detection of changeable risk factors for stroke could result in better prevention of first and recurring episodes of cerebrovascular disease. One of the risk factors that can be reduced easily, safely, effectively and affordably is homocysteine levels. This makes it important to find out the frequency of hyper-homocysteinaemia among ischaemic stroke patients.

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.⁴ Many studies have shown an association between increased homocysteine level and a risk for atherosclerotic vascular disease.⁵ Similarly studies have also reported a relationship between homocysteine levels and stroke.⁶ Moreover, stroke patients with hyper-homocysteinaemia have more frequently developed cerebral microangiopathy and multiple infarctions compared to patients with normal homocysteine serum level.⁷ This clearly shows that homocysteine levels can have important public health consequences.

However, most of the data present in the literature is of the western population and till now very few studies have been done in the Pakistani population. The lifestyle, eating habits and genetic profiles of the Pakistani population may differ from the other data in the literature, thus justifying this study. The main purpose of this study was to find out the frequency of hyper-homocysteinaemia in Pakistani patients with ischaemic stroke and its relation with other risk factors, as this is a modifiable factor that may help in formulating strategies in reducing stroke incidence and its complications.

Patients and Methods

The cross-sectional study based on convenience

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sampling was conducted at the Civil Hospital, Karachi, from May to July 2012. Ischaemic stroke patients were conveniently selected from the Out-patient Department (OPD) and Emergency Department (ED) of the hospital after taking informed consent from each patient as well as well ethical approval from the College of Physicians and Surgeons of Pakistan (CPSP). The sample size was calculated using Open Epi, taking p as 0.48 at 95% confidence interval (CI).⁸ Ischaemic stroke was defined as neurological deficit lasting more than 24 hours with either a normal Computed Tomography (CT) of brain or evidence of infarct on CT brain done within 1 week of onset. Patients with known ischaemic heart disease, previous history of ischaemic strokes, peripheral vascular disease, hypothyroidism and epilepsy were excluded. Pregnant females and patients taking drugs that might affect homocysteine, vitamin B12, or folate metabolism such as multivitamins, niacin, methotrexate, tamoxifen, anticonvulsants, bile acid sequestrants, or nitrous oxide anaesthesia were also excluded.

An overnight 8-hour fasting venous blood sample (4ml in ethylenediaminetetraacetate[EDTA]) was drawn, and sent to Dow University of Health Sciences (DUHS) laboratory for analysis. Samples were analysed on AxSYM analyzer using Abbott's kit by fluorescent polarisation method. Rest of the data was collected through a structured proforma and was analysed using SPSS 17.0. Frequencies and percentages were calculated for categorical variables including gender, smokers, history of diabetes mellitus and hypertension, hyper-homocysteinaemia and mode of admissions. Mean \pm Standard Deviation (SD) was computed for age and homocysteine values. Analysis of variance (ANOVA) was used to compare the mean homocysteine levels between stroke patients who smoked or were diabetic or had hypertension. ANOVA was also used to compare the homocysteine levels between different age groups of stroke patients.

Results

The mean age of the 96 patients in the study was 64.9 ± 10.9 years (range: 40-85). Of the total, 12(12.5%) patients had age over 79 years, while 55(57.3%) were between 60 and 79 years. The remaining 29(30.2%) patients were in the 40-59 age bracket (Table-1). Besides, 67(69.8%) patients were males, while 29(30.2%) were female, and 84(87.5%) of the total cases were enrolled from the OPD. Overall, 69 (71.9%) patients were hypertensive, while 31(32.3%) were diabetic, and 19(20%) were smokers. Hyper-homocysteinaemia was found in 56(58.3%), and 40(41.7%) had normal homocysteine

Table-1: Frequency of stroke patients according to age groups.

Age groups of participants	Frequency	Percentage	Cumulative percentage
40-59 years	29	30.2	30.2
60-79 years	55	57.3	87.5
Greater than 79 years	12	12.5	100

Table-2: Frequency of hyper-homocysteinaemia among ischaemic stroke patients.

Homocysteine level among stroke patients	Frequency	Percentage
≤ 15 mmol/L	40	41.7
> 15 mmol/L	56	58.3

Table-3: Mean homocysteine levels of stroke patients in different sub-groups.

Variables	Sub groups	No of Patients (%)	Homocysteine levels (Mean \pm S.D)	P-value
Gender	Male	30(53.6)	16.01 \pm 1.4	0.152
	Female	26(46.4)	15.5 \pm 1.2	
Age (Years)	40 - 59	15(26.8)	16.9 \pm 1.6	0.239
	60 - 79	29(51.8)	17.7 \pm 1.3	
	> 79	12(21.4)	17.6 \pm 0.9	
Co-morbidity	Hypertension	27(48.2)	16.8 \pm 1.4	0.263
	Diabetes Mellitus	16(28.6)	16.2 \pm 1.1	
	Smokers	13(23.2)	15.9 \pm 1.6	

levels (Table-2).

The difference along gender lines was not statistically significant ($p < 0.57$). Out of the 56 cases of hyper-homocysteinaemia, 30(53.6%) patients were male and 26(46.4%) were female. Moreover, mean homocysteine levels also showed no significant difference ($p < 0.152$) in gender terms. Mean homocysteine level in males was $16.01 \pm 1.4 \mu\text{mol/L}$, while females had a mean of $15.5 \pm 1.2 \mu\text{mol/L}$.

The frequency was significantly high in the age 60-79 age group ($p < 0.007$). However, mean homocysteine levels showed no significant difference between different age groups ($p < 0.239$). The age group containing patients of over 79 years of age had the highest homocysteine levels of $17.6 \pm 0.9 \mu\text{mol/L}$, while the homocysteine levels in the age groups of 40-59 and 60-79 were $16.9 \pm 1.6 \mu\text{mol/L}$ and $17.7 \pm 1.3 \mu\text{mol/L}$ respectively (Table-3).

As for co-morbidities, there was no statistically significant difference ($p < 0.263$) in the mean homocysteine levels among stroke patients who smoked or had hypertension or diabetes.

Discussion

The study observed a strong link between hyper-homocysteinemia and ischaemic stroke. More than half of our ischaemic stroke patients (58.3%) had hyper-homocysteinemia. The findings are supported by a recent study which showed that hyper-homocysteinemia was found in 48% of ischaemic stroke patients and, hence, suggested homocysteine as an individual risk for ischaemic stroke.⁸

In another study, hyper-homocysteinemia was found in 50% of stroke patients but only less than 5% of the population had high levels of homocysteine. Approximately in 30% of stroke patients, serum homocysteine level was 1.5 times higher compared to healthy individuals of similar age and gender. Moreover, stroke patients with hyper-homocysteinemia more frequently developed cerebral microangiopathy and multiple infarctions compared to patients with normal homocysteine serum level.⁷ However, some researches have failed to determine any link between hyper-homocysteinemia and stroke.⁹

In our study, males had a higher homocysteine levels than females. One study also reported that males were found to have higher homocysteine levels than females.¹⁰ In an Indian study, difference of homocysteine levels between males and females were statistically insignificant.¹¹ A few studies have also shown that homocysteine levels increase with age.¹⁰ This finding can be elucidated on the basis of nutritional status, vitamin intake that is likely to decrease with increase in age. However, in a different research, no relation was found between homocysteine levels and age.¹¹ In our study also, there was no significant relationship between homocysteine levels and age.

There has been inconsistent data regarding relation between homocysteine and hypertension. Some studies failed to establish any relation,¹² while others have reported relation between hypertension and homocysteine levels.¹¹ In our study, the homocysteine levels were higher in hypertensive ischaemic stroke. It is proposed that hyper-homocysteinemia induces an elastolytic process in the arterial wall by inducing synthesis and secretion of serine elastase. The loss of elastin may lead to the stiffening of the arterial wall, resulting in hypertension. This might be one of the factors by which hyper-homocysteinemia contributes as a risk factor for stroke, although other concomitant factors may also exist.¹³

Our study showed high homocysteine levels in smokers. Hyper-homocysteinemia was found in 23.2% of stroke patients who were smokers. Many authors have found

that tobacco smoking is positively correlated with high homocysteine levels.¹⁴ Similarly, the Hordaland Homocysteine study¹⁵ concluded that people who smoked had a markedly elevated plasma homocysteine levels that amplified around linearly with the number of cigarettes smoked daily. However, a negative association was observed by one study.¹³ More studies are required to inspect whether quitting smoking can decrease homocysteine levels. Similarly, increased homocysteine concentrations were found in 28.6% of stroke patients who were diabetic. In other studies, conflicting results have been found regarding association between homocysteine levels and diabetes mellitus.¹⁶ This further re-emphasises the need for more research studies to observe the association between homocysteine levels and diabetic stroke patients.

If high homocysteine levels are confirmed to be an independent risk factor for stroke in future studies, it can have major health implications because homocysteine levels can be easily reduced through simple measures. For instance, studies have shown that vitamin B12 supplementation of even 0.4mg can lower the homocysteine levels by 7%. Moreover, folic acid supplementation (0.5 to 5mg) can reduce homocysteine levels by one quarter.^{17,18} Similarly, other dietary measures such as increased vitamin B6 supplementation, high dietary taurine and trimethylglycine (TMG) supplements can all have a favourable effect on homocysteine levels and, therefore, might have protective roles in vascular diseases.^{19,20}

This study had many strong points. One of them was that all possible confounders of homocysteine levels were present in the exclusion criteria and the patients were carefully excluded from the study if they had any confounder of homocysteine levels. Secondly, it used fasting blood samples for levels of homocysteine as non-fasting blood samples in previous studies have shown raised homocysteine levels.¹³ However, the sample size in our study was relatively small. Hence, further studies should be done in other parts of the country as well.

Conclusion

Hyper-homocysteinemia is a modifiable risk factor that is associated with a high number of ischaemic stroke patients in the Pakistani population. Prevention of hyper-homocysteinemia will reduce the incidence of stroke and ultimately lessen the prevalence of ischaemic stroke in Pakistan.

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