Frequency of Homocysteinemia in Ischemic Stroke Patients

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ABSTRACT

Background: Stroke is a form of cardiovascular disease affecting the blood supply to the brain, resulting in neurologic deficit in the corresponding area of the body. Epidemiologic studies have identified homocysteinemia as a possible risk factor for atherosclerosis. It was ranked as the second most common cause of death and the third most common cause of disability in the world by WHO in 2010.

Objective: To assess the frequency of homocysteinemia in patients of ischemic stroke and determine relationship between homocysteinemia and other factors like age, sex, hypertension, diabetes and smoking.

Material and Methods: A single centered cross sectional study which included100 patients of ischemic stroke admitted in the department of Medicine, Benazir Bhutto Hospital Rawalpindi in 2016.

Results: The mean age of patients was 59.06 ±11.501 years and the mean serum homocysteine level of the patients was 15.38 ± 6.93 m mol/dl. There were 35 patients having homocysteinemia with ischemic stroke while in 65 patients homocysteine level was within normal range. The presence of homocysteinemia was found to be significantly more in non-diabetics ($p< 0.02$) and normotensive ($p<0.001$) patients as compared to diabetic and hypertensive patients respectively. The presence of homocysteinemia in smokers and non-smokers was not statistically significant ($p=0.151$).

Conclusion: The frequency of homocysteinemia was 35% in patients of ischemic stroke in our study and was more in non-diabetics and normotensive patients.

Further large, multi-center trials are required to demonstrate the relationship between homocysteinemia and other diseases.

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INTRODUCTION

Stroke is a form of cardiovascular disease affecting the blood supply to the brain resulting in neurologic deficit in the corresponding area of the body, weakness on clinical examination with decreased power, hyperreflexia, a positive Babinski's sign, and a hypodense or hyperdense area on CT scan brain. Acute ischemic stroke is caused by thrombotic or embolic occlusion of a cerebral circulation and it is much more common than hemorrhagic type. WHO statistics show that about 15 million people suffer from stroke worldwide each year out of which about 5 million people die and another 5 million become permanently disabled.[1] In Pakistan this crippling disease was estimated to have an incidence of 179-216 per 100,000 people, while its mortality was 52-85 per 100,000 people in the year 2010.[1]

It has been reported reported that, more than 40% of patients have a poor outcome, defined as being dead, dependent, or institutionalized three months after stroke.[2,3]

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In another study after performing autopsies on many patients, Kilmer McCully found that elevated levels of homocysteine were directly related to various vascular lesions in these individuals and he further postulated that moderately elevated homocysteine due to heterozygous mutations in homocysteine related genes or poor vitamin status also lead to increased risk of cardiovascular disease.[4]

In a meta-analysis of contrasting persons and homocysteine levels over the 90thpercentile to the rest, the risk ratio for coronary artery disease was found to be 1.7, for cerebrovascular disease 2.5, for peripheral vascular ailment 6.8, and for venous thrombosis 2.95. In addition, it was found that an increase of 5.0 mmol/L in homocysteine level, the hazard of CAD increased by as much as increase of cholesterol by 20 mg/dL.[5] In another Hordaland homocysteine study including 2127 men and 2639 women, between 65 and 67 years of age included for a cardiovascular screening program demonstrated that an increase of 5 mmol/L in plasma homocysteine level was associated with a 49% increase in mortality and 50% increase in cardiovascular mortality. On the other hand homocysteinemia was not found to be a risk factor for atherosclerosis by the American Heart Association which was due to low frequency of Homocysteinemia, (5-7% only) in the American population.[5,6]

The present study was aimed to assess the frequency of homocysteinemia in patients of ischemic stroke and determine relationship between homocysteinemia and other factors like age, sex, hypertension, diabetes and smoking.

MATERIAL AND METHODS

This was a cross-sectional study in which 100 patients of ischemic stroke fulfilling inclusion criteria were included in the six months' time i.e. from January to June 2016. Subjects were recorded through non-Probability, consecutive sampling admitted within 24 hours of onset of stroke to the department of Medicine, Benazir Bhutto Hospital Rawalpindi, both male and female aged 18-75 years. Critically ill patients on ventilator support or with hemorrhagic stroke, stroke due to cerebral venous sinus thrombosis, atrial fibrillation, known valvular heart disease and pregnant women were not included in the study.

Ethical Approval

Permission for data collection was taken from the Ethical committee of the Hospital through proper channel.

Data Collection Procedure

A total number of 100 newly diagnosed patients of ischemic Stroke were selected from medical units of Benazir Bhutto Hospital, Rawalpindi. Written consent was taken from first degree relatives of patients. A complete history was taken including biography and risk factors like diabetes, hypertension and smoking. An overnight 8-hour fasting 4ml venous blood sample in ethylenediaminetetraacetate (EDTA) tube was taken, and sent to uniform laboratory for analysis by Formosa Biomedical technology Total Homocysteine Biochemical Assay Kit was used for determination of serum homocysteine levels.

The normal reference range of Homocystein was taken as 5-15 um/L. The data was analysed by using SPSS Version 23. Quantitative data like age and homocysteine levels were presented as means and standard deviations. Frequency and Percentage was determined for homocysteine. P values was analyzed for levels of homocysteine in patients of stroke. Percentages and P values for effect modifiers like, hypertension, diabetes and smoking were controlled by stratification. Post stratification chi-square test was applied. .

RESULTS

A total of 100 patients were included in this study. The mean age of patients was 59.06±11.501 years and the mean Serum homocysteine level was 15.38±6.93mmol/dl. There were 41 female patients (41%)while 59 patients were male (59%). 53 patients (53%) were hypertensive, 51 patients (51%) were diabetic and 44 patients (44%) were smokers.There were 35 (35%) patients having homocysteinemia with stroke while in 65 (65%) patients of ischemic stroke, homocysteine levels was normal.

Comparison was done between the presence of homocysteinemia and other diseases including diabetes, and hypertension using chi-square test. The presence of Homocysteinemia was found to be significantly more in non-diabetic ($p<0.02$) and normotensive ($p<0.001$)patients as compared to diabetic and hypertensive patients respectively. The presence ofhomocysteinemia in smokers and non-smokers was not statistically significant ($p=0.151$). The stratification was done according toageandgender.

Table-1: Frequency of Homocysteinemia in Patients.

Homocysteinemia	Frequency	%age
Negative	65	65.0
Positive	35	35.0
Total	100	100.0

Table 2. Comparison of Homocysteinemia between hypertensive and normotensive patients suffering from ischemic stroke.

	Hypertension		p-value
Homocysteinemia	**Normotensive**	**Hypertensive**	
Negative	**25 (53.2%)**	**40 (75.5%)**	
Positive	**22 (46.8%)**	**13 (24.5%)**	**<0.02**
Total	**47 (47%)**	**53 (53%)**	

Table 3. Comparison of homocysteinemia between diabetic and non-diabetic patients of ischemic stroke.

	Diabetes		p-value
Homocysteinemia	**Non-Diabetic**	**Diabetic**	
Negative	**22 (44.9%)**	**43 (84.3%)**	
Positive	**27 (55.1%)**	**8 (15.7%)**	**<0.001**
Total	**49 (49%)**	**51 (51%)**	

DISCUSSION

The prevalence of homocysteinemia in patients suffering from stroke has been reported to be different in different studies. In our study the homocysteinemia was seen in 35% of patients having ischemic stroke wheras 65% of patients had normal levels of homocysteine. In a study conducted in Karachi, the frequency of homocysteinemia was found to be 58 (3%)[7]. The similarity of high prevalence with our study is clear evidence that there is a strong relationship between homocysteinemia and ischemic stroke. The findings are supported by a recent study conducted in China which showed that high levels of homocysteine were found in patients of ischemic stroke in young patients and, hence, suggested homocysteine as an individual risk for ischemic stroke.[8] Ischemic stroke patients with homocysteinemia more frequently developed cerebral microangiopathy and multiple infarcts compared to patients with normal homocysteine level. However, some researches have different results and they do not find any relationship of cardiovascular events with high levels of homocysteine.[9]

In our study, males had slightly higher homocysteine levels than females which is similar to a study conducted in 2007 in China by Hao L et al who showed that males are more prone to have homocysteinemia compared to females.[10] Some studies have shown that homocysteine levels increase with increasing age. [11] This finding can be elucidated on the basis of nutritional status, vitamin and folic acid intake that is likely to decrease with increase in age. In our study there was significant relationship between homocysteinemia and age.

There is variable relationship between hypertension and homocysteinemia. Some studies failed to establish any relation while others have reported relation between hypertension and homocysteine levels. [12] In our study, the homocysteine levels were higher in hypertensive ischemic stroke as compared to normotensive.

Homocysteinemia was found in 23.2% of stroke patients who were smokers in our study which was not significantly high. Some authors have linked the relationship of smoking with homocysteinemia while other studies found no significant relation, as in our study. One study conducted at national level however showed that smokeless tobacco rather than smoking was associated with homocysteinemia. [13] There is conflicting evidence in previous studies depicting association of homocysteinemia with smoking.

Homocysteine levels are modifiable with simple dietary changes. There has been conflicting evidence that Vitamin B6, B12 and folate supplements have impact on reducing cardiovascular events by reducing homocysteine level.[10,14-16]

Screening of patients earlier with additional risk factors may help in reducing the risk of developing stroke and this can prove beneficial in public health sectors in the management of ischemic stroke. More studies are required to show homocysteinemia to be an independent risk factor.

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CONCLUSION

Homocysteinemia was found to be 35% in patients of ischemic stroke in our study.

Further large, multi-center trials are required to demonstrate the relationship between homocysteinemia and other diseases.

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