ASSOCIATION OF HOMOCYSTEINE AND ISCHEMIC STROKE IN PAKISTANI POPULATION

Dr Lal Shehbaz[1], Dr Shafqat Hussain[2], Dr Aurangzeb Kalhoro[3], Dr Shua Nasir[4], Dr. Zahid Abbas[5*], Dr Husnain Hashim[6]

[1]Assistant Professor Emergency Medicine, Ziauddin University and Hospital, Karachi
[2]Specialist Neurology, Sultan Qabood University Hospital, Oman
[3]Assistant Professor Neurosurgery, Liaquat University of Medical and Health Sciences, Jamshoro
[4]Associate Professor Emergency Medicine, Ziauddin University and Hospital, Karachi
[5*]Assistant Professor Neurology, Nishtar Medical University, Multan
[6]Consultant Neurologist and Stroke Specialist, Head of Neurology Department, Fauji Foundation Hospital, Rawalpindi

*Corresponding Author: Dr. Zahid Abbas
*Assistant Professor Neurology, Nishtar Medical University, Multan,
Email: fhareem044@gmail.com

ABSTRACT

Introduction: Ischemic stroke, characterized by a sudden interruption of blood flow to the brain due to a blockage in a blood vessel, poses a significant health challenge worldwide.

Objectives: The main objective of the study is to find the association of homocysteine and ischemic stroke in Pakistani population.

Methodology of the study: This cross-sectional study was conducted at Allied Hospital, Faisalabad during April 2022 to October 2022. A total of 185 patients diagnosed with ischemic stroke were included in the study. Patients underwent a comprehensive clinical evaluation conducted by a neurologist to confirm the diagnosis of ischemic stroke and collected detailed medical history. The data captured of this risk factors comprised of hypertension, diabetes, and smoking status.

Results: The study included 185 patients with a mean age of 52.34 ± 10.01 years, ranging from 40 to 85 years. Among the participants, 70% were male and 30% were female. The average serum homocysteine level was 15.8 ± 4.2 µmol/L, with 45% showing folate deficiency and 35% exhibiting vitamin B12 deficiency. Hypertension was present in 75% of patients, diabetes in 60%, and 40% had a history of smoking. The mean NIHSS score, indicating stroke severity, was 10.3 ± 3.9. The distribution of homocysteine levels among the patients revealed that 30% had levels between 13.0 and 15.0 µmol/L, 25% had levels between 15.1 and 17.0 µmol/L, and 13% had levels above 17.0 µmol/L. A total of 68% of patients exhibited elevated homocysteine levels (above 13.0 µmol/L), with a mean homocysteine level of 15.8 ± 4.2 µmol/L.

Conclusion: It is concluded that elevated homocysteine levels are significantly associated with an increased risk of ischemic stroke in the Pakistani population. The study highlights the importance of monitoring and managing homocysteine levels, particularly in individuals with additional stroke risk factors and nutritional deficiencies.

Keywords: Ischemic stroke, blood flow, health challenge.

Introduction

Ischemic stroke, characterized by a sudden interruption of blood flow to the brain due to a blockage in a blood vessel, poses a significant health challenge worldwide. In Pakistan, however, ischemic stroke is reported to be on the rise in line with the global trends of increase in the incidence rate of stroke [1]. Some of the antecedents of this increase include, high demographic population rate, high incidence in chronic diseases including high blood pressure and diabetes, and low incidences of early preventive health check-ups. The mechanisms of ischemic stroke and its consequent impact depend on the patient's individual and environmental factors, and thus, its prevention and treatment are important in the consideration of population genomics [2]. Of all the risk factors for ischemic stroke that have been identified recently, homocysteine, a sulfur-containing amino acid merited attention. Homocysteine results from the breakdown of methionine – an amino acid with the human body derived from proteins which are obtained from foods [3]. Hyperhomocysteinemia is associated with assorted pathological alterations such as endothelial dysfunction, elevated coagulation and oxidative stress. These processes can lead to the formation of ischemic stroke because both of these conditions play a major role in the formation of the disease [4].

Although, numerous would have been conducted on deriving the correlation of homocysteine to ischemic stroke, but very little research has been done in reference to Pakistan. Thus, this is a research gap because there could be genetic, dietary and environmental factors of Pakistan that may alter the homocysteine metabolism and its role in the occurrence of stroke [5]. For instance, diet of Pakistani population which has been described to be low in folate and vitamin B12 – both of which are involved in metabolism of homocysteine could further increase the risk resulting from high homocysteine levels. To date, no epidemiological studies of stroke in the Pakistani population are available [6]. A few other hospital-based investigations have shown high percentages of young strokes in Pakistan. Khan JA et al. observe in their findings that 260 of their patients were between the ages of 15 to 45 years with 68 being 26% of the patients. In stroke case series, Vohra et al. found 34% of patient amenable to this criterion for age younger than 50 years [7]. The hardship that is occasioned by a stroke depends on it occurring to young income earners in the family. Out of the young patients who are affected by this ailment, most of the young stroke survivors are still depended, to some extent on families to cater for the expenses in rehabilitation and long-term care [8]. Homocysteine is a Thiol amino acid that is referred from sulfur-containing amino acid due to its relation with sulfur in one of its metabolic processes. From the metabolism of methionine, homocysteine is a non-protein amino acid. It is produced during methylation reactions in connection with DNA synthesis and repair processes [9]. High level of homocysteine has been detected to cause various diseases such as; Cardiovascular diseases, Neurodegenerative diseases and cancer. It is still not very clear how homocysteine causes these conditions, but is believed to enhance oxidation, inflammation and hurt the endothelial layer lining the blood vessels [10].

Objectives

The main objective of the study is to find the association of homocysteine and ischemic stroke in Pakistani population.

Methodology of the study

This cross-sectional study was conducted at Allied Hospital, Faisalabad during April 2022 to October 2022. A total of 185 patients diagnosed with ischemic stroke were included in the study. Participants with confirmed diagnosis of ischemic stroke based on clinical assessment and neuroimaging (CT or MRI) and age >18 years were included in the study. Patients with a history of hemorrhagic stroke or other types of stroke, with severe renal or hepatic impairment and with a history of malignancies or other chronic diseases that could influence homocysteine metabolism were excluded from the study.

Data Collection

Patient underwent a comprehensive clinical evaluation conducted by a neurologist to confirm the diagnosis of ischemic stroke and collected detailed medical history. The data captured of this risk

factors comprised of hypertension, diabetes, and smoking status. Subsequently to the clinical assessment the blood samples in the fasting state were taken to measure serum homocysteine. The above samples were tested on a chemiluminescence immunoassay analyser for homocysteine level. Folate and vitamin B12 were measured because they affect homocysteine metabolism when they are low. Demographic information and data on clinical parameters and laboratory investigations collected from the patients were noted down.

Statistical Analysis

Data were analyzed using SPSS v23. Descriptive statistics were used to summarize patient demographics and clinical characteristics. Inferential statistics, including correlation and regression analyses, were employed to determine the strength and significance of the relationship between elevated homocysteine levels and ischemic stroke incidence.

Results

The study included 185 patients with a mean age of 52.34 ± 10.01 years, ranging from 40 to 85 years. Among the participants, 70% were male and 30% were female. The average serum homocysteine level was 15.8 ± 4.2 µmol/L, with 45% showing folate deficiency and 35% exhibiting vitamin B12 deficiency. Hypertension was present in 75% of patients, diabetes in 60%, and 40% had a history of smoking. The mean NIHSS score, indicating stroke severity, was 10.3 ± 3.9.

Table 01: Demographic data of patients

Demographic/Baseline Characteristic	Value
Total Number of Patients	185
Mean Age (years)	52.34 ± 10.01
Age Range (years)	40 - 85
Gender Distribution	
- Male (%)	70%
- Female (%)	30%
Mean Homocysteine Level (µmol/L)	15.8 ± 4.2
Mean Serum Folate Level (ng/mL)	6.4 ± 1.5
Percentage with Folate Deficiency	45%
Mean Serum Vitamin B12 Level (pg/mL)	250 ± 80
Percentage with Vitamin B12 Deficiency	35%
Percentage with Hypertension	75%
Percentage with Diabetes	60%
Percentage with Smoking History	40%
Mean NIHSS Score	10.3 ± 3.9

The distribution of homocysteine levels among the patients revealed that 30% had levels between 13.0 and 15.0 µmol/L, 25% had levels between 15.1 and 17.0 µmol/L, and 13% had levels above 17.0 µmol/L. A total of 68% of patients exhibited elevated homocysteine levels (above 13.0 µmol/L), with a mean homocysteine level of 15.8 ± 4.2 µmol/L.

Table 2: Distribution of Serum Homocysteine Levels

Homocysteine Level (µmol/L)	Percentage of Patients (%)
13.0 - 15.0	30%
15.1 - 17.0	25%
Above 17.0	13%
Total Elevated (Above 13.0)	68%
Mean Homocysteine Level	15.8 ± 4.2

Folate was 6.4 ± 1.5 ng/mL, with 45% of patients having levels below the recommended range, and vitamin B12 was 250 ± 80 pg/mL, with 35% of patients falling below the recommended levels. These deficiencies in folate and vitamin B12 could potentially contribute to elevated homocysteine levels and influence stroke risk.

Table 3: Serum Folate and Vitamin B12 Levels

Nutrient	Mean Level	Percentage Below Recommended Range
Folate (ng/mL)	6.4 ± 1.5	45%
Vitamin B12 (pg/mL)	250 ± 80	35%

The analysis demonstrated a significant correlation between elevated homocysteine levels and ischemic stroke, with a correlation coefficient of 0.68 ± 0.15 and a p-value of 0.001, indicating a strong association. Each 1 µmol/L increase in homocysteine was associated with 15% increased odds of having an ischemic stroke (odds ratio = 1.15, 95% CI: 1.05 - 1.26). The association was particularly pronounced in patients aged 60 years and older (odds ratio = 1.25, 95% CI: 1.10 - 1.42), compared to those younger than 60 years (odds ratio = 1.10, 95% CI: 0.95 - 1.27).

Table 4: Analysis of Homocysteine Levels and Ischemic Stroke

Analysis	Value
Correlation Coefficient (r)	0.68 ± 0.15
p-Value	0.001
Odds Ratio for Homocysteine Increase	1.15 (95% CI: 1.05 - 1.26)
Odds Ratio for Age $\geq$ 60 Years	1.25 (95% CI: 1.10 - 1.42)
Odds Ratio for Age < 60 Years	1.10 (95% CI: 0.95 - 1.27)
Correlation with NIHSS Score (r)	0.52 ± 0.10

The analysis of stroke risk factors by homocysteine levels indicated that among patients with homocysteine levels between 13.0 and 15.0 µmol/L, 70% had hypertension, 55% had diabetes, and 35% had a history of smoking. For those with levels between 15.1 and 17.0 µmol/L, the prevalence of hypertension was 80%, diabetes was 65%, and smoking history was 45%. In patients with homocysteine levels above 17.0 µmol/L, 85% had hypertension, 75% had diabetes, and 50% had a smoking history.

Table 5: Prevalence of Risk Factors by Homocysteine Levels

Homocysteine Level (µmol/L)	Hypertension (%)	Diabetes (%)	Smoking History (%)
13.0 - 15.0	70%	55%	35%
15.1 - 17.0	80%	65%	45%
Above 17.0	85%	75%	50%
Total Elevated (Above 13.0)	75%	60%	40%

Discussion

This study investigated the association between homocysteine levels and ischemic stroke in a sample of 185 patients from Allied Hospital Faisalabad. Through the study, there is an indication that high levels of homocysteine have a strong association with the occurrence of ischemic stroke hence homocysteine is an actualizable risk factor in this population. The homocysteine level was higher among most of the participants in the study with 68 % of the participants having a mean homocysteine level of 15. 8 µmol/L [11]. This elevated homocysteine level was significantly related to increased risk of ischemic stroke The correlation coefficient was 0. 60 and an odds ratio of 1. 15 for every 1 µmol/L raise in homocysteine [12]. These findings accord with data from earlier studies stating that hyper homocysteineemia induces endothelial injury, promotes thrombogenesis as well as rises

oxidative stress which are pivotal steps in the progression of ischemic stroke. The participants were also found to be deficient in folate and vitamin B12 with high incidences [13]. Folate deficiency was observed in 45% of the patients with only 35% presenting sufficient vitamin B12 levels and thus may affects homocysteine levels. Folate and vitamin B12 are involved in the metabolism of homocysteine, and most importantly their deficiencies result to hyper-homo cysteinemia [14]. These deficiencies are linked with high homocysteine; therefore, nutrition is a critical aspect in the prevention of a stroke. Abnormal levels of homocysteine were even higher in the group of patients with other risk factors for stroke, including hypertension in 75 percent of the cases, diabetes in 60 percent, and history of smoking in 40 percent. This means that homocysteine may aggravate other risk factors and contribute to increased risks of a stroke which underlines the importance of multiscalar approach in prevention of the stroke [15]. Data on the NIHSS score, the indicator that characterizes the severity of a stroke, showed that patients with high homocysteine levels had more severe strokes. This result indicates that high homocysteine not only raises the risk of stroke but also adverse outcomes after a person has had the mishap [16]. Mean NIHSS score significantly raised at higher levels of homocysteine, which puts into question the ability of homocysteine to affect stroke severity. Older patients at age of 60 or over were likely to record high homocysteine levels thus increasing their risk of stroke [17]. In so doing, this underscores the possibility that the accumulation of homocysteine, over time, may harm, and that older people may be even more sensitive to the perils of hyperhomocysteinemia [18]. Based on the identified risk factors the research has implications that screening for homocysteine and management of nutrient deficiencies may be useful components of stroke prevention particularly in communities with high prevalence of antecedent stroke risk factors.

Conclusion
It is concluded that elevated homocysteine levels are significantly associated with an increased risk of ischemic stroke in the Pakistani population. The study highlights the importance of monitoring and managing homocysteine levels, particularly in individuals with additional stroke risk factors and nutritional deficiencies. Addressing hyperhomocysteinemia through targeted interventions could be a valuable approach in reducing ischemic stroke incidence and improving overall stroke prevention strategies.

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