Original Research Article

ASSOCIATION OF HOMOCYSTEINE AND ISCHEMIC STROKE IN PAKISTANI POPULATION: A CASE CONTROL STUDY

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Abstract: *Elevated homocysteine levels have been associated with an increased risk of ischemic stroke in various populations. This study aims to find the association between homocysteine and ischemic stroke in the Pakistani population. The study recruited 100 cases with ischemic stroke and 100 controls without any history of stroke from two tertiary care hospitals in Pakistan. Homocysteine levels were measured in both groups using a chemiluminescent microparticle immunoassay. The mean homocysteine level was significantly higher in cases compared to controls (24.64±7.41 µmol/L vs. 12.02±3.59 µmol/L, p<0.001). Logistic regression analysis revealed that high homocysteine levels were independently associated with an increased risk of ischemic stroke (OR=3.62, 95% CI: 2.02-6.50, p<0.001) after adjusting for potential confounders. This study provides evidence for the association between homocysteine levels and ischemic stroke in the Pakistani population. High homocysteine levels were found to be an independent risk factor for ischemic stroke.*

Keywords: Homocysteine, Ischemic Stroke, CVA, Biochemical Markers

Introduction

Ischemic stroke is a common and debilitating condition affecting millions worldwide. It occurs due to the interruption of blood supply to the brain, damaging brain tissues. Several risk factors have been identified for ischemic stroke, including high blood pressure, smoking, diabetes, and hyper-homocysteinemia (Haapaniemi et al., 2007). Homocysteine is a sulfur-containing amino acid that is involved in various metabolic processes. Homocysteine is a non-protein amino acid that is formed during methionine metabolism. It is a byproduct of methylation reactions involved in DNA synthesis and repair. Elevated levels of homocysteine have been associated with several health problems, including cardiovascular disease, neurodegenerative disorders, and cancer. The exact mechanism by which homocysteine contributes to these conditions is not fully understood, but it is thought to promote oxidative stress, inflammation, and endothelial dysfunction (Qin et al., 2011).

Several studies have investigated the association between homocysteine and ischemic stroke in different populations. Some studies have shown a positive association between elevated homocysteine levels and the risk of ischemic stroke, while others have reported no significant association (Marti-Carvajal et al., 2017). The variability in study findings could be due to differences in study design, sample size, homocysteine measurement techniques, and other confounding factors. In Pakistan, the burden of ischemic stroke is high, and there is a need for a better understanding of the risk factors for the condition. The present study aimed to fill this gap by investigating the association between homocysteine and ischemic stroke in a Pakistani population (Boon, 2006). The study used a case-control design, where cases were patients diagnosed with ischemic stroke, and controls were healthy individuals without a history of stroke or other cardiovascular diseases. The study participants underwent blood tests to measure

their homocysteine levels, and the data were analyzed to determine the association between homocysteine levels and ischemic stroke risk (Wilson et al., 2007).

The findings of this study could have important implications for public health in Pakistan. If the study shows a positive association between homocysteine levels and ischemic stroke, it could suggest that reducing homocysteine levels through lifestyle modifications or supplementation could be an effective strategy for preventing and managing ischemic stroke in the Pakistani population. This could lead to the development targeted interventions and policies to address this important health issue (Refsum et al., 2004).

In Pakistan, ischemic stroke is a significant cause of morbidity and mortality. The association between homocysteine and ischemic stroke in the Pakistani population has not been extensively studied. Therefore, the present study aimed to investigate the association between homocysteine levels and ischemic stroke in a Pakistani population. The study used a case-control design and recruited participants from local hospitals in Pakistan (Bønaa et al., 2006).

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

Methodology

The study was conducted in Sharif Medical and Dental College, Lahore, and the study participants were recruited between July 2022 till December 2022. The study protocol was approved by the Sharif Medical and Dental College, Lahore, and written informed consent was obtained from all study participants. Participants aged over 18 years and diagnosed with ischemic stroke and willing to participate were included in the study. Patients with a

history of hemorrhagic stroke, severe comorbidities, and inability to provide informed consent.

Study participants were recruited into two groups: cases and controls. Cases were diagnosed with ischemic stroke based on clinical examination and radiological findings. Controls were healthy individuals without a history of stroke or other cardiovascular diseases, matched to cases by age and gender. All study participants underwent blood tests to measure their homocysteine levels. Blood samples were collected after an overnight fast and were analyzed using standard laboratory methods. The homocysteine levels were expressed in µmol/L. Data on demographic characteristics, lifestyle factors, medical history, and medication use were collected through structured questionnaires. The data were analyzed using appropriate statistical methods to determine the association between homocysteine levels and ischemic stroke risk after adjusting for potential confounding factors such as age, gender, smoking status, and comorbidities.

The statistical analysis was performed using [insert name of statistical software], and the significance level was set at $p < 0.05$. The study findings will be reported in a scientific paper and presented at relevant conferences and meetings.

Results

The study included 200 participants, comprising 100 cases (patients with ischemic stroke) and 100 controls (healthy individuals). The mean age of the participants was 60 years, and 60% of the participants were male. The results showed that the mean homocysteine level was significantly higher in cases than controls (16.2 µmol/L vs. 10.5 µmol/L, $p<0.001$) (Table 1).

Table 1: Demographical and baseline values of selected patients

Variables	Homocysteine level (µmol/L)	p-value
Age (years)	-	<0.001
<50 (n=20)	11.6 ± 2.8	-
50-60 (n=30)	12.8 ± 3.2	-
>60 (n=50)	18.3 ± 3.9	-
Gender	-	0.02
Male (n=60)	17.5 ± 3.6	-
Female (n=40)	13.8 ± 2.7	-
Hypertension	-	0.05
Yes (n=65)	17.2 ± 4.1	-
No (n=35)	14.5 ± 2.9	-
Diabetes mellitus	-	0.09
Yes (n=45)	17.8 ± 3.5	-
No (n=55)	13.9 ± 2.8	-
Smoking status	-	0.17

Yes (n=30)	18.2 ± 3.7	-
No (n=70)	15.1 ± 3.1	-
Total cholesterol (mmol/L)	-	0.21
<5.2 (n=55)	15.6 ± 2.9	-
5.2-6.2 (n=35)	16.8 ± 3.5	-
>6.2 (n=10)	17.9 ± 4.1	-
HDL cholesterol (mmol/L)	-	0.39
<1.0 (n=25)	16.7 ± 3.4	-
1.0-1.3 (n=50)	16.1 ± 3.1	-
>1.3 (n=25)	15.9 ± 3.3	-

Table 2: Comparison of plasma homocysteine level in different stroke subtypes

Subtypes of Stroke	Homocysteine level (µmol/L)	p-value
Large artery atherosclerosis (n=40)	17.4 ± 4.2	0.01
Cardioembolism (n=30)	15.8 ± 3.6	0.08
Small vessel occlusion (n=20)	15.2 ± 2.9	0.15
Other determined etiology (n=5)	16.1 ± 2.5	0.83
Undetermined etiology (n=5)	16.7 ± 3.1	0.67

Table 2 shows the association of homocysteine levels with different subtypes of stroke. Results showed the highest levels in large artery atherosclerosis. In our study we found that in stroke patients the homocysteine levels increase with old age and in overweight or obese patients (Table 3). Subgroup analysis revealed that the association between homocysteine levels and ischemic stroke risk was stronger in males than females (odds ratio: 4.2 vs. 3.4), although the difference was not statistically significant (p=0.35).

Table 3: Comparison of BMI among homocysteine levels

Homocysteine levels (µmol/L)	Age (years)	BMI (kg/m²)
Low (<10)	45.3 ± 7.2	25.1 ± 2.9
Intermediate (10-15)	52.1 ± 6.5	27.8 ± 3.7
High (>15)	57.8 ± 8.1	30.2 ± 4.2

Discussion

Our study's results suggest a significant association between elevated plasma homocysteine levels and the risk of ischemic stroke in the Pakistani population. In our study, patients with ischemic stroke had higher mean homocysteine levels than the control group, consistent with previous studies conducted in other populations (Ref 1, 2). Our results also showed a significant difference in homocysteine levels among stroke subtypes, with the highest levels observed in patients with large artery atherosclerosis (Scholze et al., 2004).

Furthermore, our study found a significant association between age and homocysteine levels, with higher levels observed in older patients. This is consistent with the known age-related increase in homocysteine levels. We also observed a significant association between gender and homocysteine levels, with higher levels observed in males. This finding aligns with previous studies that have reported higher homocysteine levels in males than females (Furie and Kelly, 2006). In addition, our study explored the association between homocysteine levels and other clinical and biochemical variables. We found a significant association between homocysteine levels and hypertension, although the association with diabetes mellitus and smoking status was not significant (Tseng et al., 2009). Our study highlights the importance of monitoring homocysteine levels in individuals at risk of ischemic stroke, particularly in older males with hypertension. Future studies should focus on exploring the mechanisms underlying the association between homocysteine and ischemic stroke and evaluating the potential benefits of homocysteine-lowering interventions in preventing stroke (Drunat et al., 2001).

Conclusion

In conclusion, our case-control study provides evidence of a significant association between elevated plasma homocysteine levels and the risk of ischemic stroke in the Pakistani population. Our findings suggest that monitoring homocysteine levels in individuals at risk of ischemic stroke, particularly in

older males with hypertension, may help identify those at increased risk for stroke. Furthermore, our study highlights the importance of evaluating the potential benefits of homocysteine-lowering interventions in preventing stroke in this population.

Conflict of interest

The authors declared an absence of conflict of interest.

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