Original Research Article

Homocysteine Levels in Acute Ischemic Stroke

ABSTRACT

Objective: The objective of this study was to determine the frequency of elevated homocysteine levels in acute ischemic stroke patients presenting to the medical department, civil hospital, Nawabshah. **Methodology:** A cross-sectional study was conducted at the Department of Medicine Civil Hospital, Nawabshah from 13/02/2021 to 12/08/2021. It included ischemic stroke patients and evaluated their homocysteine levels (≥15μmol/L were elevated). Homocysteine levels was compared then in relation with the other sub-groups of patients based on the age group, gender and obesity, smoking, hypertensive and diabetic status, and hyperlipidemia. **Results:** There were 171 (64.5%) males and 94 (35.5%) females with mean age 49.9 ± 5.8 years Elevated levels of homocysteine were recorded in 140 (52.8%) patients with acute ischemic stroke. The frequency of elevated levels of homocysteine across various subgroups of patients in relation to age, gender, obesity, smoking, hypertension, diabetes, and hyperlipidemia was found to be insignificant. **Conclusion:** The findings of this study show patients with acute ischemic stroke had elevated levels of homocysteine which suggests potential implications of homocysteine level assessment in the diagnostic workup as well as risk stratification and management planning of patients with acute ischemic stroke presenting in future medical practice.

Keywords: Acute Ischemic Stroke, Chi-square test, Homocysteine, Nawabshah.

INTRODUCTION

Stroke is a medical emergency and happens either due to loss of blood supply or reduced blood supply to the brain resulting in oxygen and nutrient depletion to the brain tissue. American Heart Association/American Stroke Association (AHA / ASA) has characterized the stroke as a neurological deficit due to vascular causes (hemorrhage or infarct) in the central nervous system [1]. It is among the most major causes of disabilities and mortality all around the world[2]. Ischemic and hemorrhagic stroke are two major types. Ischemic stroke accounts for 80% of the cases while hemorrhagic stroke is only 20% of the cases[3]. Homocysteine is an amino acid that is derived through the metabolic demyelination of dietary methionine. Its normal levels in the blood are around 5-12mmol/L. If it is raised above 12mmol/L, it can cause oxidative damage to the endothelium of the vessels that leads to an activation of prothrombin[4]. Homocysteine levels

are considered as a predictor of neurological deficits in patients having an acute ischemic stroke as it has been strongly linked with vascular disease[5]. Similarly, several studies have also shown a strong relationship between homocysteine levels and stroke[6]. The neurological deficits seen in stroke patients having elevated levels of homocysteine as compared to the patients with normal levels of homocysteine include cerebral microangiopathy and multiple infarctions[7].

The studies show that hyperhomocysteinemia increases the chances of having a thromboembolic condition but it is still not clear which subtype of stroke is associated with hyper-homocysteinaemia[8]. In one of the studies, 75% of the ischemic stroke patients were found to have elevated fasting homocysteine levels[9] while in another study, 76.66% cases of ischemic stroke were revealed to have high fasting homocysteine levels as compared to normal people[10].

Therefore, this study aims to find out the significance of the level of homocysteine in patients developing acute ischaemic stroke and the frequency of ischemic stroke patients with elevated homocysteine levels as there is lacking the evidence in the Pakistani population. It will help to diagnose the risk factor of stroke early which can be avoided in our population.

METHODOLOGY

A cross-sectional study was conducted at the Department of Medicine Civil Hospital, Nawabshah. The duration of the study was 6 months after the approval of the synopsis from 13/02/2021 to 12/08/2021. The sample size of 265 cases was calculated with a 95% confidence interval and 6% margin of error while taking the expected frequency of elevated homocysteine levels to be 55.0% in patients with acute ischemic stroke[11]. Patients were selected by non-probability, consecutive sampling. The inclusion criteria of the study were all acute ischemic stroke patients presenting within 48 hours, both gender (Male and Female), Age 40-60 years while the exclusion criteria were patients presenting with recurrent stroke, hemorrhagic stroke, and ischemic stroke patients presenting after 48 hours of the onset of symptoms.

All cases fulfilling the inclusion criteria during the study period were enrolled after written informed consent obtained. Demographic and baseline details of the study subjects like age, gender (male and female), time and date of admission, presenting complaints, obesity, smoking, hypertension, hyperlipidemia, and diabetes were noted and recorded into the attached questionnaire. ECG and CT / MRI findings were noted. After that 5 ml of the blood was drawn under aseptic measures and total homocysteine levels in the blood were measured in the laboratory.

The data collected was entered on the latest version of SPSS and analyzed. The numerical variables including age and BMI have been presented by mean ±SD. The categorical variables(i.e.gender, history of smoking, diabetes, hyperlipidemia, hypertension, obesity, and elevated homocysteine levels) have been shown in terms of the frequency and percentage. The data is then stratified for the age group, gender, obesity, diabetes mellitus, smoking, hyperlipidemia, and hypertension in order to find the significances of the factors that modify the

effect. After the stratification, further tests including the chi-square test was applied with a p-value ≤0.05 as significant.

RESULTS

The patient's age varies from 40 years t 60 years and the mean age was 49.9±5.8 years. Additionally, among all the cases,171 (64.5%) males and 94 (35.5%) females with a male to female ratio of 1.8:1 were found. The BMI of the patients included in our study varied from 22.2 Kg/m^2 to 34.8 Kg/m^2 with a mean of 30.4±3.4 Kg/m^2. 76 (28.7%) patients were obese. 209 (78.9%) patients were hypertensive while 72 (27.2%) patients were a smoker. 104 (39.2%) patients were diabetic while 96 (36.2%) patients had hyperlipidemia as shown in Table 1.

Table 1. Baseline Characteristics of Study Sample

Characteristics	**Participants** **n=265**
Age (years)	
Mean	49.9 ± 5.8
≤50 years	129 (48.7%)
>50 years	136 (51.3%)
Gender	
Male	171 (64.5%)
Female	94 (35.5%)
BMI (Kg/m2)	
Mean	30.4 ± 3.4
Non-Obese	189 (71.3%)
Obese	76 (28.7%)
Hypertension	
Yes	209 (78.9%)
No	56 (21.1%)
Smoking	

Yes	72 (27.2%)
No	193 (72.8%)
Diabetes Mellitus	
Yes	104 (39.2%)
No	161 (60.8%)
Hyperlipidemia	
Yes	96 (36.2%)
No	169 (63.8%)

Elevated levels of homocysteine were recorded in 140 (52.8%) patients with acute ischemic stroke which is represented in the Table 2.

Table 2. Frequency of Elevated Levels of Homocysteine in Patients with Acute Ischemic Stroke (*n=265)*

Elevated Levels of Homocysteine	**Frequency (n)**	**Percent (%)**
Yes	140	52.8%
No	125	47.2%
Total	265	100.0%

Additionally, the frequency of elevated levels of homocysteine across various subgroups of patients in relation to age (p-value=0.970), gender (p-value=0.930) and obesity (p-value=0.615), smoking (p-value=0.992), hypertensive (p-value=0.860) and diabetic (p-value=0.790) status and hyperlipidemia (p-value=0.559) was found to be insignificant that has been exhibited in Table 3.

Table 3. Comparison of Elevated Levels of Homocysteine across Various Subgroups of Patients with Acute Ischemic Stroke (*n=265)*

Subgroups	**n**	**Elevated Homocysteine n (%)**	**P-value**
Age			
≤50 years	129	68 (52.7%)	0.970

>50 years	136	72 (52.9%)	
Gender			
Male	171	90 (52.6%)	0.930
Female	94	50 (53.2%)	
BMI			
Non-Obese	189	98 (51.9%)	0.615
Obese	76	42 (55.3%)	
Hypertension			
Yes	209	111 (53.1%)	0.860
No	56	29 (51.8%)	
Smoking			
Yes	72	38 (52.8%)	0.992
No	193	102 (52.8%)	
Diabetes Mellitus			
Yes	104	56 (53.8%)	0.790
No	161	84 (52.2%)	
Hyperlipidemia			
Yes	96	53 (55.2%)	0.559
No	169	87 (51.5%)	

Chi-square test, observed difference was statistically insignificant

DISCUSIION

Globally, 13.7 million people are affected by stroke every year and it is the second leading cause of death-causing 5.5 million death annually[12]. This topic has been researched broadly all around the first. Initially, Robi et al studied this topic on 77 patients with non-lacunar stroke and failed to detect any variation in the levels of homocysteine levels[13]. On the contrary, Yao et al analyzed the data of 194 acute ischemic stroke patients to study the significance of homocysteine levels.

He found out that the levels of homocysteine were elevated and were highly associated with ICH[14].

We observed in our study a relative male predominance in patients, presenting with acute ischemic stroke, with a male to female ratio of 1.8:1. Our observation is in line with that of other local studies where Ahmad et al. (1.8:1)[15], Khan et al. (1.8:1)[16], Taj et al. (1.9:1)[17], and Khalid et al. (2.2:1)[18] reported similar male predominance in local population with stroke. Renjen et al. in 2015 also reported a male-female ratio of 1.8:1 in the Indian population[19]. The same male-female ratio of 2.1:1 with the male being predominant is also reported by Bhowmik et al. in 2016 in Bangladeshi patients with stroke[20].

The 28.7% of patients with acute ischemic stroke were obese in our study. The findings of our study are in line with the observation of Aly et al.[21] who reported the frequency of obesity to be 26.6% among stroke patients at Agha Khan University Hospital, Karachi. Khalid et al.[18] reported it to be 23.7% at the same institute while Khan et al.[22] reported it to be 23.8% in such patients at Al-Junaid Hospital, Nowshera. In our study, 78.9% of stroke patients were hypertensive, 27.2% of patients were smokers, 39.2% patients were diabetic and 36.2% patients had hyperlipidemia. The findings are consistent with that of Ahmad et al.[15] reporting almost the same proportion of patients having hypertension (70.8%) and diabetes mellitus (39.2%) in stroke patients in the local population.

The major finding in our study was that elevated levels of homocysteine were recorded in 140 (52.8%) patients with acute ischemic stroke. There was no statistically significant difference in the frequency of elevated levels of homocysteine across various subgroups of patients based on age (p-value=0.970), gender (p-value=0.930) and obesity (p-value=0.615), smoking (p-value=0.992), hypertensive (p-value=0.860) and diabetic (p-value=0.790) status and hyperlipidemia (p-value=0.559).Similar results were found in a local study where Zaheer et al. evaluated blood homocysteine levels of 37 patients presenting with ischemic stroke at Mayo Hospital Lahore and reported the frequency of hyperhomocysteinemia to be 51.4%[23]. Rehman et al. in another similar local study conducted at Shaikh Zayed Hospital, Lahore reported raised levels of homocysteine among 51.0% of patients with ischemic stroke[24].

The major limitation of our study was that it included data from a single hospital. If such a study would be multicentred and included diversity in the population, the results would have been more accurate.

CONCLUSION

In the present study, a substantial proportion of patients with acute ischemic stroke had elevated levels of homocysteine which suggests potential implications of homocysteine level assessment in the diagnostic workup as well as risk stratification and management planning of patients with acute ischemic stroke presenting in future medical practice.

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