# ORIGINAL ARTICLE Frequency of Hyperhomocysteinemia in Young (≤45 years) patients presenting with Acute Ischemic Stroke at Tertiary Care Hospital, Karachi

NAEEMULLAH BULLO<sup>1</sup>, AAISHA AZIZ<sup>2</sup>, MUNIR AFZAL<sup>3</sup> <sup>1,3</sup>Assistant Professors, Department of Neurology, Jinnah Postgraduate Medical Center/JSMU Karachi <sup>2</sup>Rabia Moon Memorial Institute of Neuroscience (Trust) Karachi Correspondence to Dr. Nameeullah Bullo, E-mail: bullonaeem@hotmail.com, Cell: 0300-2576335,

# ABSTRACT

Aim: To determine the frequency of hyperhomocysteinemia in young (≤ 45 years) patients presenting with acute ischemic stroke at Tertiary Care Hospital, Karachi.

**Methodology:** The cross-sectional study was conducted at Department of Neurology and Medicine, Jinnah Postgraduate Medical Center Karachi from 1<sup>st</sup> February 2021 to 31<sup>st</sup> July 2021. Patients' data was collected after a verbal consent was obtained. The diagnostic criteria were met by 119 cases.

**Results:** Mean age, duration of acute ischemic stroke, body mass index, height, weight and homocysteine level were  $38.41\pm4.58$  years,  $6.54\pm3.91$  hours,  $28.66\pm3.51$  kg/m<sup>2</sup>,  $151\pm10.25$  cm,  $71.8\pm11.69$  kg and  $10.7\pm3.42$  µmol/L. Fifty four (45.4%) and 65 (54.6%) were male and female. Fifty nine (49.6%) and 60 (50.4%) had and did not have hyperhomocysteinemia.

**Conclusion:** 49.6% of young stroke patients had hyperhomocysteinaemia, a modifiable risk factor for ischemic stroke. Therefore close monitoring of patients must be done in all patients with regular follow-up.

**Keywords:** Acute ischemic stroke, Young patients, Hyperhomocysteinemia

## INTRODUCTION

Stroke is a debilitating illness that affects millions of people worldwide. It is caused by the interruption of blood flow to the brain, leading to damage or death of brain cells<sup>1</sup>. Its incidence in Asia has been increasing recently, according to a rough estimate<sup>1</sup>. Pakistan is one of the Asian nations hardest hit by this dreadful disease, contributing to exponential demands on financial resources, community services, health care and the economy. According to recent statistics, stroke is the third leading cause of death in Pakistan, with over 200,000 cases reported annually<sup>2</sup>. The impact of stroke on the economy is also significant. The cost of treatment and rehabilitation for stroke patients can be expensive, which puts a strain on the healthcare system and the country's overall budget. Additionally, many stroke survivors are unable to return to work or require long-term care, which further adds to the economic burden<sup>3,4</sup>.

Hyperhomocysteinemia is a condition where there are high levels of homocysteine in the blood. Homocysteine is an amino acid that is produced during the metabolism of methionine, an essential amino acid. High levels of homocysteine have been linked to various health problems, including cardiovascular disease and stroke<sup>5.6</sup>. A prothrombotic environment is created by high homocysteine levels' effects on platelets, thrombin and fibrin, oxidative damage to the vascular endothelium, and an increase in vascular smooth muscle growth<sup>7</sup>. Niazi et al<sup>6</sup> examined acute ischemic stroke patients for hyperhomocysteinemia and found a prevalence of 50.2%

The purpose of the study is to evaluate the prevalence of hyperhomocysteinemia in young (≤45 years) patients with acute ischemic stroke. The identification of modifiable risk factors, such as homocysteinemia, could lead to better stroke prevention and prevent young patients from becoming incapacitated as a result of stroke. Furthermore, in the light of the information gained from this study, an effective treatment plan will be developed that places the importance on homocysteinemia.

## MATERIALS AND METHODS

The cross sectional study was conducted at Department of Neurology and Medicine, Jinnah Postgraduate Medical Center (JPMC), Karachi, from 1<sup>st</sup> February 2021 to 31<sup>st</sup> July 2021. All patients both gender, age between 20 to 45 years were newly diagnosed young acute ischemic stroke patients presenting within

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24 hours, confirmed through CT-scan showing hypodense area were included. Patients with a history of hemorrhagic stroke, venous sinus thrombosis and use of oral contraceptives or medications that affect the metabolism of vitamin B12 or folate, renal impairment, chronic obstructive pulmonary disease, asthma, congestive heart failure, myocardial infarction, or chronic liver disease were excluded from the study. Record a medical history of disease duration and demographic information collected at the time of admission from the patient or companion in case of aphasia or low GCS. The admitted patient's CT scan was performed and the scan, which showed hypodense area was labelled as ischemic stroke. Physical examination was performed to assess muscle power, aphasia, imbalance, and GCS to label ischemic stroke. The blood sample was collected 5ml disposable syringe and 5ml of blood was drawn from the peripheral vein and collected in a specific tube for measuring serum homocysteine levels at the time of admission. Data was analyzed on SPSS Version 20.

# RESULTS

The mean age was 38.41±4.58 years. Whereas, mean duration of acute ischemic stroke, body mass index, height, weight and homocysteine level were 6.54±3.91 hours, 28.66±3.51 kg/m<sup>2</sup>, 151±10.25cm, 71.8±11.69 kg and 10.7±3.42 µmol/L respectively. Out of 119 ischemic stroke patients, 59 (49.6%) and 60(50.4%) had and did not have hyperhomocysteinemia and 25 (21%) patients observed in 20-40 years while 94 (79%) patients were in 41-60 years. Ninety nine (83.2%) and 20(16.8%) had urban and rural residence respectively. Forty (33.6%) and 79(66.4%) had duration of acute ischemic stroke <12 hours and >12 hours respectively. Twenty nine (24.4%) and 90 (75.6%) had and did not have diabetes mellitus type II respectively. 30(25.2%) and 89(74.8%) had and did not have hypertension respectively. 19 (16%) and 100(84%) had and did not have dyslipidemia respectively. Forty seven (39.5%) had smoked and 72(60.5%) did not smoke respectively. Fifty nine (49.6%) had obesity and 60 (50.4%) did not have obesity respectively. Sixty eight (57.1%) patients had anemia and 51(42.9%) had not anemia respectively. There were 11 (9.2%), 44(37%) and 64(53.8%) were in monthly income of < 25000, 25001-50000 and > 50001 respectively. Sixty eight (57.1%) were employed and 51(42.9%) were unemployed. Seven (5.9%), 12(10.1%), 46(38.7%) and 54(45.4%) were in illiterate, primary, secondary and higher respectively (Table 1).

Thirteen (22%) cases were in 20-40 years where as 46(78%) cases in 40-60 years with p-value was 0.48. Hyperhomocysteinemia in 23(39%) cases observed in male whereas 36(61%) cases in were in female. Hyperhomocysteinemia

was observed in 4(83.1%) cases had urban residence while 10(16.9%) cases had rural residence and P-value was 0.58.

Variable	No.	%
Gender		
Male	54	45.38
Female	65	54.62
Age (years)		
20 – 40	38	32.48
41 – 60	81	67.52
Duration of acute ischemic stroke	(hours)	
< 12	40	33.61
> 12	79	66.39
Residence		
Urban	99	83.19
Rural	20	16.81
Diabetes mellitus		
Yes	29	24.37
No	90	75.63
Hypertension		
Yes	30	25.21
No	89	74.79
Dyslipidemia		
Yes	19	15.97
No	100	84.03
Smoking		
Yes	47	39.50
No	72	60.50
Obesity		
Yes	59	49.58
No	60	50.42
Anemia		
Yes	68	57.14
No	51	42.86
Occupation		
Employed	68	57.14
Unemployed	51	42.86
Hyperhomocysteinemias		
Yes	59	49.58
No	60	50.42

Table 2: Stratification of hyperhomocysteinemia according to different variables (n=119)

Variable	Hyperhomocysteinemia		Trial			
	Yes	No	lotal	P value		
Gender						
Male	23 (39%)	31 (51.7%)	54 (45.4%)	0.11		
Female	36 (61%)	29 (48.3%)	65 (54.6%)			
Age (years)						
20 – 40	13 (22%)	12 (20%)	25 (21%)	0.49		
41 – 60	46 (78%)	48 (80%)	94 (79%)	0.40		
Duration of acute ischemic stroke (hours)						
< 12	21 (35.6%)	19 (31.7%)	40 (33.6%)	0.39		
> 12	38 (64.4%)	41 (68.3%)	79 (66.4%)			
Residence						
Urban	49 (83.1%)	50 (83.3%)	99 (83.2%)	0.59		
Rural	10 (16.9%)	10 (16.7%)	20 (16.8%)	0.56		
Diabetes mellitus						
Yes	12 (20.3%)	17 (28.3%)	29 (24.4%)	0.21		
No	47 (79.7%)	43 (71.7%)	90 (75.6%)			
Hypertension						
Yes	14 (23.7%)	16 (26.7%)	30 (25.2%)	0.43		
No	45 (76.3%)	44 (73.3%)	89 (74.8%)			
Dyslipidemia						
Yes	6 (10.2%)	13 (21.7%)	19 (16%)	0.07		
No	53(89.8%)	47(78.3%)	100 (84%)			
Smoking						
Yes	27 (45.8%)	20 (33.3%)	47 (39.5%)	0.11		
No	32 (54.2%)	40 (66.7%)	72 (60.5%)			
Obesity						
Yes	29 (49.2%)	30 (50%)	59 (49.6%)	0.53		
No	30 (50.8%)	30 (50%)	60(50.4%)			
Anemia						
Yes	35 (59.3%)	33 (55%)	68 (57.1%)	0.20		
No	24 (40.7%)	27 (45%)	51 (42.9%)	0.30		
Occupation						
Employed	33 (55.9%)	35 (58.3%)	68 (57.1%)	0.46		
Unemployed	26 (44.1%)	25 (41.7%)	51 (42.9%)	0.40		

Duration of acute ischemic stroke with respect to hyperhomocysteinemia observed 21(35.6%) cases in had the

acute ischemic stroke for <12 hours where as patients who had the acute ischemic stroke for > 12 hours in 38(64.4%) cases with P-value was 0.39 (Table 2).

#### DISCUSSION

A medical emergency known as an acute ischemic stroke happens when blood supply to the brain is interrupted, which causes brain cells to be damaged and eventually die. One potential risk factor for acute ischemic stroke is homocysteine metabolism. Homocysteine is an amino acid that is produced during the breakdown of proteins in the body. Elevated levels of homocysteine have been linked to an increased risk of cardiovascular disease, including stroke. This may be due to homocysteine's ability to damage blood vessels and promote blood clotting<sup>9,10</sup>.

There are unclear explanations for how homocysteine may raise the risk of vascular disease<sup>11</sup>. However, vitro research suggests that homocysteine may have a procoagulant effect by modifying tissue plasminogen activator (tPA) activity and influencing von Willebrand factor (vWF) secretion<sup>12</sup>.

Young stroke patients showed high tissue plasminogen mass concentration but low tissue plasminogen activity and plasminogen activator inhibitor-1 (PAI-1) activity, according to recent research. It is therefore of interest to investigate possible associations between homocysteine levels and fibrinolytic factors.<sup>13</sup> Mean age, duration of acute ischemic stroke, body mass index, height, weight and homocysteine level in our study was  $38.41\pm4.58$  years,  $6.54\pm3.91$  hours,  $28.66\pm3.51$  kg/m<sup>2</sup>,  $151\pm10.25$  cm,  $71.8\pm11.69$  kg and  $10.7\pm3.42$  µmol/L respectively.

In a prospective study of young patients with ischemic stroke at the Pakistan Atomic Energy Commission Hospital in Islamabad, the median age of the 71 participants was 35.8 years. A total of 36 (50.7%) cases had hyperhomocysteinemia. The incidence was significantly higher in males and in the 36-45 year age group (63.4%). Homocysteine levels had no significant impact on discharge outcomes<sup>14</sup>.

Hyperhomocysteinemia is thought to cause an elastolytic development in the arterial wall. High blood pressure can be caused by hardening of the arterial wall caused by a lack of elastin. Although there may be other reasons, this can be one of the causes of hyperhomocysteinemia as a risk factor for stroke. Regarding the link between high homocysteine levels and diabetes mellitus, several researches have produced inconsistent findings. It is now well established that B vitamin therapy lowers tHcy levels, which may result in a reduced risk of stroke.<sup>15,16</sup> The risk of stroke and myocardial infarction are both decreased by tHcy-lowering therapy with B vitamins, according to a number of recent studies and meta-analyses. According to studies, a 0.4 mg vitamin B12 supplement can reduce homocysteine levels by 7%. Moreover, supplementing with folic acid (0.5 to 5 mg) can lower homocysteine levels by one-fourth<sup>15,16</sup>.

The average homocysteine levels in the present study was 16.80 6.71 micromol/L. Regardless of age, gender, or diabetes mellitus, patients with ischemic stroke had high homocysteine levels. In comparison to non-hypertension participants, hypertensive subjects had greater homocysteine levels (P<0.05)<sup>17</sup>.

### CONCLUSION

Hyperhomocysteinemia, a modifiable risk factor for ischemic stroke, was observed in about 49.58% of young stroke patients. Stroke in young patients requires a comprehensive investigation of all possible causes. It is a large cohort of systematic studies to determine whether homocysteine-lowering therapy with high doses of folic acid, pyridoxine, and vitamin B12 actually lowers the incidence of stroke in young patients, given that hyperhomocysteinemia has been linked to an increased incidence of stroke. **Conflict of interest:** Nil

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