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Homocysteine as a Predictor of Early Neurological Deterioration in Acute Ischemic Stroke

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Abstract

Background: Ischemic stroke (AIS) is on the rise owing in part to a longer average life expectancy. It's called early neurological deterioration (END) when symptoms deteriorate immediately after the stroke, and it's connected with a decreased probability of recovery. As homocysteine levels rise, so does the risk of neurotoxicity and other conditions that contribute to thrombosis. There are a number of ways that homocysteine may be hazardous, including direct toxicity and endothelium damage, according to experiments. If homocysteine could predict early neurological impairment after an ischemic stroke, this research would have been a success. Patients with acute ischemic stroke were included in the trial at Mataria teaching Hospital (AIS). The participants in the study were, on average, 63 years old and 12 months old. Two-thirds of the participants were men (60.0 percent). The majority of individuals had hypertension (86.0 percent). One-fifth of research participants had diabetes mellitus (52.0 percent) More over a third of the participants admitted to smoking cigarettes (44.0 percent). More than one-third of the participants had dyslipidemia and coronary artery disease (approximately a quarter). The average HbA1c level in this research was 5.8%, with a standard variation of 1.3 percentage points.. It varied from a low of 2 to a high of 176, with an average of 11.5. Some 42.0 percent of the participants had elevated homocysteine concentrations. Age (P-value = 0.657), gender (P-value = 0.368), hypertension (P-value = 0.075), diabetes mellitus (P-value = 0.086), smoking (P-value = 0.171), and dyslipidemia (P-value = 0.726) were found to be non-significant variations across the groups. There was a statistically significant association between early neurological deterioration and a higher median CRP (47.5) compared to those with no decrease (10). Homocysteine levels were greater in individuals with early neurological degeneration (786%) than in those without deterioration (278%) (P = 0.001). Age (P=0.056), gender (P=0.815), high blood pressure (P=0.009), diabetes mellitus (P=0.603), or high cholesterol (P=0.863) were not linked to low homocysteine levels. HbA1C (P=0.507), CRP (P=0.643), or elevated lipid profiles (P=0.603) did not vary across the groups. Because of our investigation, we discovered a substantial connection between elevated levels of homocysteine and END. Homocysteine levels in acute stroke patients might be used as a prognostic indicator for such individuals.

Key words: Homocysteine, Predictor, Early Neurological Deterioration, Acute Ischemic Stroke

1. Introduction

Acute Ischemic stroke (AIS) is becoming more common, in part because people are living longer. Since the 1990s, intravenous tissue plasminogen activator (IV TPA) has been the only proven therapy for persons with AIS (IV tPA). It was shown that intra-arterial thrombolysis (IAT) is safe and efficacious if provided within six hours of symptoms start for MCA occlusions, according to PROACT II investigation. Second IMS research looked at whether intravenous and intraarterial therapy could be safely combined in patients with acute ischemic stroke (AIS) after the first IMS experiment. [1]

One of the most common signs of early neurological decline (END), which occurs rapidly after stroke, is a decrease in the patient's ability to walk or speak following the stroke. Percentage ranges from 2.2% up to 37.5% based on both severity criteria and time since previous examination. Within 24–48 hours after admission, a two-point increase on the National Institutes of Health Stroke Scale (NIHSS) is considered a stroke. Sepsis, thrombosis extension, excitotoxic effects, and inflammation all play a role in lacunar infarction, but may have a higher influence on the disease's course than other components [2].

Imaging techniques like MR and CT perfusion can reveal the extent of ischemic tissue during an acute stroke, but these advanced imaging methods are not always available. Individuals in need of further imaging, monitoring, and/or early intervention may be more easily identified with the use of simple risk prediction at the first clinical exam. It is common for END in the acute phase of Ischemia-Septic Shock to lead to a considerable increase in disability and death rates after reperfusion treatment. High blood sugar levels at the time of admission, neurological dysfunction, high systolic blood pressure, fibrinogen and a delay between admission and treatment have all been linked to an increased chance of developing End-stage Renal Disease (END). A sulfhydryl-containing amino acid, this amino acid is primarily produced and degraded in the liver. Having high levels of plasma homocysteine is a symptom of deficiency in folate or cobalamin and a risk factor for cardiovascular disease. Homocysteine may produce neurotoxicity and be connected to other pro-thrombotic variables if the levels are too high. Experimental investigations suggest that a variety of processes, including direct toxicity and damage to the vascular endothelium, may be responsible for homocysteine toxicity. In individuals with stable or acute coronary artery disease, increased homocysteine levels have also been linked to poor outcomes, according to some research [7]. In a few studies, homocysteine has been connected to functional impairment in the acute period after stroke. Acute stroke effects such as End are not known to be connected with high homocysteine levels.

In order to explore whether homocysteine may be used to predict early neurological impairment

following an ischemic stroke, the study's aim was to test this theory.

2. Patients and Methods

A. Technical design

1- Study type and region:

This The research was carried out at the Mataria Teaching Hospital's Neurology Department.

2- The study's target population is the following:

Acute ischemic stroke patients from Mataria Teaching Hospital were included in the research (AIS)

Number of people having acute ischemic stroke: fifty (AIS).

Male and female participants are required to meet the following requirements:

• Over the age of 18

Criteria for exclusion:

A variety of conditions may affect a patient, including:

If you have kidney or liver problems.

Myocardial infarction, uncontrolled angina, ventricular aneurysm, and congestive heart failure.

• Dangerous condition.

Blood vessel abnormalities and aneurysm.

Stroke with bleeding.

• Surgery on the brain

carotid endarterectomy or stenting of the carotid artery in the past.

The following information was gathered from each patient upon admission as part of the operational design:

Initiation of the process i.

In addition to taking a complete history, this includes:

Name, age, marital status and address are some of the personal details that should be included in this section.

Smoking, diabetes, high blood pressure, and coronary artery disease are all risk factors.

3. A history of past surgeries or hospitalizations, if any.

Drugs taken by patients, if known.

A history of any sickness in the family.

II. A clinical evaluation aimed at:

Examine the following:

• A general assessment of the patient's mental and emotional well-being.

Signs of life (Blood pressure, Temperature, Heart rate, Respiratory rate, capillary filling time).

• Symptoms of (Pallor, Cyanosis, Jaundice, and Lymph node enlargement).

Edema of the lower limbs.

B. Comprehensive examination, which includes:

Detection of any aberrant heart sounds or murmers is done by the cardiovascular system.

Any aberrant breath sound, extraneous noises, or respiratory distress may be detected by the respiratory system's two main functions.

The presence of organomegaly or ascites in the GIT or abdominal cavity.

4- The CNS and the Musculoskeletal System (MSS) Pupilary response, testing of the motor system (including the power, tone and reflexes), as well as an assessment of Glasgow coma score.

C. Neurological impairments are assessed.

A scale developed by the National Institutes of Health to measure the severity of stroke (NIHSS) For the NIH stroke scale, see Table 1.

Intensity of a stroke

no signs of a stroke

Minor strokes range from 1–4, moderate strokes range from 5–15, severe strokes range from 16–20, and catastrophic strokes range from 21–42.

• Investigations: On the first day of admission, all patients had the following examinations:

The results of an unplanned glucose test

- HbA1c

Tests for the kidneys and the liver

The lipid profile and the urine analysis are included in this

In terms of C-reactive protein (CRP),

homocysteine levels in blood

Preliminary brain imaging • Signs of impending neurological decline (END)

The secondary end points were determined to be END and END. Motor power or overall score increases by at least one point or two points during the first week of admission are considered ENDs. (2)

Statistical Analysis: SPSS version 22 (SPSS Inc. Chicago, IL) was used to gather, tabulate, and statistically analyse all of the data.IL, U.S.A)

3. Results

The mean age of the studied patients was 63 ±12 years. About two-thirds were males (60.0%). Most patients had hypertension (86.0%). Approximately half of the patients had diabetes mellitus (52.0%) More than one-third were smokers (44.0%). About one-third of the patients had dyslipidemia, and one-quarter had coronary artery disease (Table 1).

Table (1) General characteristics of the studied patients.

General characteristics		
Age (years)	Mean ±SD	63 ±12
Gender	Males n (%)	30 (60.0)
	Females n (%)	20 (40.0)
Hypertension	n (%)	43 (86.0)
Diabetes mellitus	n (%)	26 (52.0)
Smoking	n (%)	22 (44.0)
Dyslipidemia	n (%)	16 (32.0)
Coronary heart disease	n (%)	13 (26.0)

The mean HbA1c was 5.8 ±1.3. The median CRP was 11.5 and ranged from 2-176. About one-third had high lipid profile, and more than one-third (42.0%) had high homocysteine levels (Table 2).

Table (2) Laboratory findings of the studied patients.

Laboratory findings		
HbA1c	Mean SD	5.8 ±1.3
CRP	Median (range)	11.5 (2 - 176)
High Lipid profile	n (%)	17 (34.0)
Homocysteine level	Low n (%)	29 (58.0)
	High n (%)	21 (42.0)

CRP: C-reactive protein

The most frequent MRI brain finding was MCA (20.0%), while the least frequent findings were Tempro-occipital infarct, thalamic infarction, cerebellar infarction, and Frontal infarction (2% for each) (Table 3).

Table (3) MRI brain findings of the studied patients.

		n (%)
MRI brain	BG infarction	5 (10.0)
	Cerebellar infarction	3 (6.0)
	Occipital infarction	2 (4.0)
	Parietal infarction	5 (10.0)
	Pontine infarction	2 (4.0)
	Tempro-occipital infarct	1 (2.0)
	Tempro-parietal infarction	2 (4.0)
	Thalamic infarction	1 (2.0)
	Capsular infarction	5 (10.0)
	Cerebellar infarction	1 (2.0)
	Frontal infarction	1 (2.0)
	Lacunar infarction	9 (18.0)
	MCA	10 (20.0)
	Parieto-occipital infarction	3 (6.0)

The median NIHSS at 24 hours was 12 and ranged from 5-24, while at 7days, it was 11 and ranged from 3-2. About one-quarter of the patients had early neurological deterioration (28.0%) ***(Table 4).***

Table (4) NIHSS AT 24 hours and 7 days in the studied patients.

Outcome		
NIHSS at 24h	Median (range)	12 (5 - 24)
NIHSS at 7-day	Median (range)	11 (3 - 25)
Early neurological deterioration (END)	n (%)	14 (28.0)

No significant differences were observed between both groups regarding age (P-value = 0.657), gender (P-value = 0.368), hypertension (P-value = 0.075), diabetes mellitus (P-value = 0.086), smoking (P-value = 0.171), dyslipidemia (P-value = 0.726), and coronary artery disease (P-value = 0.329) ***(Table 5).***

Table (5) General characteristics according to early neurological deterioration.

		Early neurological deterioration		
		Yes (n = 14)	**No (n = 36)**	**P-value**
Age (years)	Mean ±SD	64 ±11	63 ±13	0.657
Gender	Males n (%)	7 (50.0)	23 (63.9)	0.368
	Females n (%)	7 (50.0)	13 (36.1)	
Hypertension	n (%)	14 (100.0)	29 (80.6)	0.075
Diabetes mellitus	n (%)	10 (71.4)	16 (44.4)	0.086
Smoking	n (%)	4 (28.6)	18 (50.0)	0.171
Dyslipidemia	n (%)	5 (35.7)	11 (30.6)	0.726
Coronary artery disease	n (%)	5 (35.7)	8 (22.2)	0.329

Independent t-test was used for age. Chi-square test was used for categorical data

The median CRP was significantly higher in those with early neurological deterioration (47.5) than those with no deterioration (10) (P-value = 0.01). High homocysteine level was significantly higher in those with early neurological deterioration (78.6%) than those with no deterioration (27.8%) (P-value = 0.001) (Table 6& figures 1).

Table (6) Laboratory findings according to early neurological deterioration.

		Early neurological deterioration		
		Yes (n = 14)	**No (n = 36)**	**P-value**
HbA1c	Mean ±SD	6.1 ±1.1	5.6 ±1.3	0.294
CRP	Median (range)	47.5 (4 - 176)	10 (2 - 52)	0.01
High Lipid profile	n (%)	5 (35.7)	12 (33.3)	0.873
Homocysteine level	Low n (%)	3 (21.4)	26 (72.2)	0.001
	High n (%)	11 (78.6)	10 (27.8)	

Independent t-test was used for HbA1C. Mann Whitney U test was used for CRP. Chi-square test was used for categorical data CRP: C-reactive protein

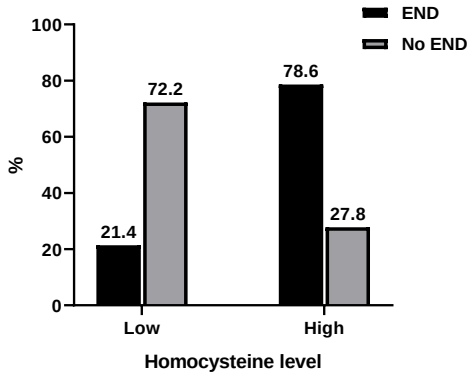

Fig.(1): Homocysteine level according to early neurological deterioration

The median NIHSS at 24 hours and 7 days was significantly higher in those with early neurological deterioration (20 and 24, respectively) than those with no deterioration (10 and 8, respectively) (P-value was < 0.001 for each) Table(7).

Table (7) NIHSS at 24 hours and 7 days according to early neurological deterioration.

		Early neurological deterioration		
NIHSS		**Yes (n = 14)**	**No (n = 36)**	**P-value**
At 24 hours	Median (range)	20 (10 - 24)	10 (5 - 19)	<0.001
At 7 days	Median (range)	24 (12 - 25)	8 (3 - 18)	<0.001

Mann Whiney U test was used

No significant difference was observed between those with low and high homocysteine level regarding age (P-value = 0.056), gender (P-value = 0.815), hypertension (P-value = 0.089), diabetes mellitus (P-value = 0.536), smoking (P-value = 0.89), dyslipidemia (P-value = 0.863), coronary artery disease (P-value = 0.764), HbA1C (P-value = 0.507), CRP (P-value = 0.643), and high lipid profile (P-value = 0.603) (Table8).

Table (8) Different parameters according to homocysteine level

		Homocysteine level		
		Low (n = 29)	**High (n = 21)**	**P-value**
Age (years)	Mean ±SD	66 ±12	59 ±12	0.056
Gender	Males n (%)	17 (58.6)	13 (61.9)	0.815
	Females n (%)	12 (41.4)	8 (38.1)	
Hypertension	n (%)	27 (93.1)	16 (76.2)	0.089
Diabetes mellitus	n (%)	14 (48.3)	12 (57.1)	0.536
Smoking	n (%)	13 (44.8)	9 (42.9)	0.890
Dyslipidemia	n (%)	9 (31.0)	7 (33.3)	0.863
Coronary heart disease	n (%)	8 (27.6)	5 (23.8)	0.764
HbA1c	Mean ±SD	5.7 ±1.3	5.9 ±1.2	0.507
CRP	Median (range)	14 (2 - 142)	10 (2.6 - 176)	0.643
High Lipid profile	n (%)	9 (31.0)	8 (38.1)	0.603

Independent t-test was used for age and HbA1C. Mann Whitney U test was used for CRP. Chi-square test was used for categorical data CRP: C-reactive protein

4. Discussion

The mean age of the patients we evaluated was 63 12 years old, according to our findings. 2/3 of those interviewed were men (60.0 percent). Hypertension was prevalent in the vast majority of individuals (86.0 percent). Patients with diabetes mellitus made up around half of the study participants (52.0 percent) more over a third of the respondents smoked (44.0 percent). One-quarter of the patients had coronary artery disease, and one-third had dyslipidemia.

The average HbA1c was 5.8 1.3. The CRP varied from 2 to 176, with a median of 11.5 points. More than a third (42.0 percent) showed elevated homocysteine levels, as did a third (33.3 percent) with an abnormal lipid profile.

In Huang et al., [5], of 220 patients with AIS, seven patients had inadequate clinical data, 189 patients had IV rt-PA for AIS, and the remaining 24 patients received EVT (11.3 percent). This resulted to a total of 213 cases being studied, with 62% of the patients having circulatory blockage in the anterior, 23% in the posterior and 17% in both branches. The average amount of time it took from the beginning of symptoms to get treatment was 3.3 hours (interquartile range [IQR] 1.9). There were 68 of 213 patients with END, 145 of whom were non-END controls.

There were 396 patients (240 males; average age of 63.5 years) enrolled for secondary analysis in Kwon et al (8). Within seven days of hospitalisation, END was diagnosed in 57 individuals (14.4 percent). Two-thirds (68 percent) of END instances occurred during the first 24 hours of hospitalisation, according to the END registry. Homocysteine levels ranged from 4.67 to 8.38 mol/L in the first quartile, from 8.39 to 10.30 mol/L in the second quartile, from 10.31 to 13.09 mol/L in the third quartile, and from 13.10 to 42.76 mol/L in the fourth quartile (fourth quartile.(

Homocysteine levels rose considerably with increasing age and male sex, as predicted (P0.05). HbA1c, high-sensitivity C-reactive protein (hs-CRP), hypertension, current smoking status, and HbA1c were not statistically significant. Diabetes, coronary artery disease, hyperlipidemia, or stroke subtype were not linked to homocysteine levels.

MCA was the most common MRI brain finding in our research, with Tempro-occipital infarction, thalamic infarct, cerebellar infarct, and Frontal infarction being the least common results (2 percent for each.(

In the first 24 hours, the median NIHSS was 12 and ranged from 5-24, whereas in the first seven days, it was 11 and varied from 3-2. One-quarter of the patients showed signs of early neurologic decline (28.0 percent).

In terms of age (P-value = 0.657), gender (P-value = 0.368), hypertension (P-value = 0.075), diabetes (P-value = 0.086), smoking (P-value = 0.171), dyslipidemia (P-value = 0.726), or coronary artery disease (P-value = 0.329), no differences between the two groups could be found between the two studies.

Before matching, Huang et al. [5] showed that diabetes mellitus was more common in the END group than in the non-END group, which is in keeping with our findings. The END group had greater TC, HDL, LDL, hyperglycemia, and the number of females, as well as worse neurologic impairment than the non-END group. No statistical differences in TC, HDL and LDL levels, diabetes, time from symptom onset to treatment, and the proportion of females were found between the two groups after matching. However, there were statistical differences in uric acid, glucose, and the NIHSS score, which were all statistically significant.

Early neurological deterioration was associated with a higher median CRP (47.5) than non-deterioration (10; P = 0.01). Early neurological deterioration patients had a considerably higher homocysteine level (78.6%) than those with no deterioration (27.8%) (P-value = 0.001.(

For 24 hours and 7 days, the median NIHSS score was considerably higher in individuals with early

neurological impairment (20 and 24, respectively) than those with no deterioration (10 and 8.(

NIHSS scores were excluded from the propensity score matching in Huang et al. [5]because the END group's scores are predicted to be higher.

People with low and high homocysteine levels were not different in age (P-value = 0.056), gender (P-value = 0.815), hypertension, diabetes mellitus, smoking (P-value = 0.89), dyslipidemia (P-value = 0.863), coronary disease, HbA1C, CRP, and high lipid profile (P-value = 0.603) when compared to those with high homocysteine levels.

As we found, (Moretti & Caruso, [6] found a link between HHCY and the incidence of stroke, ischemic or hemorrhagic, as well as cerebral haemorrhage, irrespective of previously identified risk variables such hyperlipidemia, hypertension, diabetes mellitus, and smoking.

Huang et al.,[5], found that glucose level, uric acid level (OR, 1.01; 95 percent CI, 1.00–1.02; p =0.026), and treatment approaches (EVT: OR, 3.87; 95 percent CI, 1.32–11.35; p 0.014) were significant predictors of END in the research. They also compared baseline patient characteristics between the IV rt-PA group (n = 189) and EVT group (n = 24) and found that NIHSS scores at admission [10.0 (7.0–13.0) vs 12.0 (11.0–17.5), p = 0.002] and time to treatment [3.0 (2.5–4.5) vs 4.3 (3–5.4), p = 0.024] were significantly different between the two groups. Two factors (INR and NIHSS) were significant in binary regression analysis, even after correcting for alcohol habit and time from symptom start to therapy, and remained connected with EVT.

Hyperglycemia was shown to be substantially linked with END in Huang et al., in contrast to our findings, suggesting a bad short-term prognosis [5]. One possibility might be that diabetic mice have considerably greater post-ischemic inflammatory responses and neuroprotective heat-shock chaperone gene attenuation than nondiabetic mice.

Additionally, prior studies have shown that in AIS patients with anterior circulation occlusions, hyperglycemia at admission is related with SICH after EVT, and that SICH is associated with a markedly unfavourable prognosis. Experiments on stroke models have shown that acute hyperglycemia increases brain lactate generation, causes brain edoema, breaks down the blood–brain barrier, and increases hemorrhagic transformation and infarct size, all of which may contribute to the possibility of an END developing in the future[10].

EVT was shown to be associated with an increased risk of developing END in the following years when compared to those receiving IV rt-PA (adjusted OR 3.87). In general, there are a number of explanations for his occurrence. To begin with, recent technological advancements have made EVT a viable treatment option for AIS that is less intrusive.

EVT may be useful in selected individuals with AIS who have substantial artery occlusions in the anterior circulation but not in the posterior circulation, according to new solid data from randomised clinical studies [11].

Many studies have shown that big vascular obstruction is a significant risk factor for end-stage renal disease (ESRD) [12].

There is a correlation between high HCY levels (12 mmol/L) and long-term cardiovascular events in individuals who have intracoronary BMS implants. If homocysteine levels are increased even after controlling for clinical, angiographic, and PCI-related factors; long-term clinical consequences may still be predicted. Predicting long-term outcomes following coronary artery stenting, even in randomised studies when HCY lowering medications failed to show therapeutic advantages, HCY levels remain a reliable clinical prognostic sign.

A higher median homocysteine level (median = 17, range = 5-25) was associated with a higher NIHSS score at 24 hours than a lower median homocysteine level (range = 5-20; P = 0.003). There was a significant difference between individuals with high homocysteine (median = 17; range = 5-35) and those with low homocysteine (7-day NIHSS, 8-22) on the NIHSS. (P 0.001) P 0.001

While our findings (Yao et al., 2016) indicated no differences between the two groups in terms of NIHSS scores upon admission, individuals in the low Hcy concentration group (P0.05) saw substantial improvements in their scores following a seven-day therapy period. There were 21 cases of intracranial haemorrhage (ICH) within 24 hours after receiving thrombolysis therapy. In our study, 57.1% of individuals had symptoms of ICH. P0.05) and mRS scores (P0.01) suggested poor outcomes at 3 months in patients with elevated Hcy levels (P0.05) within 24 hours.

5. Conclusion

Elevated homocysteine levels are significantly associated with END. Therefore, homocysteine levels may be valuable as a predictor of prognosis in patients with acute stroke.

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