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CORRELATION BETWEEN HOMOCYSTEINE, VITAMIN B12, FOLIC ACID LEVELS AND ACUTE STROKE: A CASE-CONTROL STUDY

Medicine

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ABSTRACT

Background: Stroke is a leading cause of morbidity and mortality worldwide, significantly impacting individuals quality of life. Elevated levels of homocysteine and deficiencies in vitamin B12 and folic acid have been identified as potential risk factors for stroke. This study aims to investigate the levels of homocysteine, vitamin B12, and folic acid in acute stroke patients compared to healthy controls, determine the prevalence of hyperhomocysteinemia, vitamin B12 deficiency, and folic acid deficiency in stroke patients, and examine the correlation between these biomarkers and stroke severity as assessed by the NIH Stroke Scale (NIHSS).

Objectives:

1) To measure and compare the levels of homocysteine, vitamin B12 and folic acid in acute stroke patients and healthy controls.
2) To determine the prevalence of hyperhomocysteinemia, vitamin B12 deficiency, and folic acid deficiency in acute stroke patients.
3) To determine if there is a correlation between the severity of stroke as assessed by the NIHSS and levels of homocysteine, vitamin B12 and folic acid.

Methodology: This case-control study was conducted at Vishwaraj Hospital, Pune. 72 Acute stroke patients confirmed by imaging (CT/MRI) were recruited during study period of 18 months. **Results:** Significantly higher homocysteine and lower Vitamin B12 level was in stroke patients compared to controls. A significant positive correlation between homocysteine levels and NIHSS scores along with negative correlation between vitamin B12 levels and NIHSS scores was observed suggesting that higher homocysteine and low vitamin B12 levels were linked to more severe strokes. **Conclusion:** The study highlight the significant correlations between vitamin B12, homocysteine levels, and stroke severity as measured by the NIHSS. Elevated homocysteine levels and lower vitamin B12 levels are strongly associated with more severe strokes.

KEYWORDS

Stroke, Homocysteine and Vitamin B12

INTRODUCTION

Stroke remains one of the leading causes of mortality and long-term disability worldwide. The World Stroke Organization has estimated that the annual global incidence of new stroke cases stands at 13.7 million. Moreover, it is projected that one in four individuals aged 25 years or older will encounter a stroke during their lifetime (1) (2). According to the Global Burden of Disease Study, India recorded approximately 1.29 million incident cases of stroke in 2019. Furthermore, the estimated annual mortality rate attributable to stroke in India is around 699,000 deaths (3). The pathophysiology of stroke is complex and multifactorial, involving a combination of genetic and environmental factors (4). Ischaemic stroke (IS) is mostly preventable.

Treatable conditions comprise around 90% of all risk factors, including arterial hypertension, diabetes mellitus, cardiac diseases, smoking, obesity, hyperlipidaemia, physical inactivity, alcohol overuse, unhealthy diet, psychosocial stress, and depression (5)(6)(7). Among the various biochemical markers studied, homocysteine, vitamin B12, and folic acid have emerged as significant contributors to stroke risk (8) (9). High levels of homocysteine can damage the blood vessels and increase the chances of blood clots, leading to ischemic stroke. Numerous studies have suggested that elevated levels of homocysteine serve as a substantial and independent risk factor for vascular diseases, including ischemic cerebral stroke (10). Vitamin B12 and folic acid play crucial roles in the metabolism of homocysteine (8)(9) (11) (12). Vitamin B12 can reduce a stroke patient's risk of having another stroke by lowering the levels of homocysteine in the blood. It also enhances stroke recovery by boosting the function and development of the brain and nerve cells (9) (11) (12). Folate, along with other B vitamins, helps break down homocysteine, an amino acid that may damage the inner walls of arteries. Such damage can boost the risk of a stroke or heart attack (11) (12) (13). Supplementing with folic acid not only has the potential to lower elevated levels of homocysteine but also demonstrates a significant ability to enhance endothelial function in patients with coronary artery disease. Conversely, deficiencies in folic acid and/or vitamin B12 can lead to hyperhomocysteinemia. Study seeks to determine the prevalence of hyperhomocysteinaemia, vitamin B12 deficiency, and folic acid deficiency in acute stroke patients. Furthermore, it aims to explore the potential correlation between the severity of stroke, as assessed by the NIHSS, and the levels of homocysteine, vitamin B12, and folic acid. Finally, the study endeavours to investigate the feasibility of using these biomarkers in predicting stroke risk.

MATERIALS AND METHODS

Study Design:

All 72 Patients with stroke (65 ischemic, 7 hemorrhagic and 5 cases of Transient Ischemic Attack (TIA) attending in-patients in Vishwaraj Hospital, Loni, Pune, whereas matched controls were identified from the relatives of the patients or cases coming for preventive check-ups, during study period of 18 months.

Inclusion Criteria for Cases (Acute Stroke Patients):

1) Patients diagnosed with acute stroke (ischemic/hemorrhagic) confirmed by imaging (CT/MRI).
2) Age ≥ 18 years.
3) Stroke occurred within the last 7 days prior to enrolment.
4) Willing and able to provide informed consent.

Inclusion Criteria for Controls (Healthy Individuals):

1) Age and sex matched individuals without a history of stroke.
2) No known neurological or psychiatric disorders.
3) Willing and able to provide informed consent.
4) No history of chronic diseases that could affect homocysteine, vitamin B12, or folic acid levels (e.g., renal failure).

Exclusion Criteria:

1) Patients with a history of chronic hematological disorders affecting vitamin B12 or folate metabolism.
2) Individuals with known B12 or folate supplementation or treatment affecting homocysteine metabolism.
3) Patients with severe comorbid conditions that could interfere with study participation or follow-up.
4) Pregnant or breastfeeding women.

5) Individuals unable to provide informed consent.

Sample Size: Cases (N=77) Controls (N=77)

Sampling Procedure: Detailed history and clinical examination was undertaken in patients, and the following investigations were done-levels of homocysteine, vitamin B12, and folic acid etc. For the stroke patients, the severity of their stroke was assessed using the NIHSS.

Statistical Analysis: Statistical analyses were conducted using IBM SPSS Version 25. Continuous variables were compared using the student's t-test or the Mann-Whitney test and categorical data were analyzed using chi-square tests. Correlations between parameters were assessed using Spearman correlation coefficient, and scatter plots were used to represent the data. A p-value of less than 0.05 was considered statistically significant, and a p-value of less than 0.01 was considered highly statistically significant.

RESULTS:

Table No. 1: Average Of Homocysteine, Vitamin B12 Level And Folic Acid Level Between Stroke Types

Marker	Stroke Type	N	Mean	SD	P
Homocysteine (umol/L)	Ischemic	65	19.8	6	0.88
	Haemorrhagic	7	19.4	7.1	
Vit B12(pg/Ml)	Ischemic	65	311.8	128.3	0.24
	Haemorrhagic	7	372.9	152.4	
Folic acid (ng/mL)	Ischemic	65	9	2.8	0.33
	Haemorrhagic	7	7.9	2.7	

The mean homocysteine level in ischemic stroke patients was 19.8 ± 6.0 µmol/L, while in hemorrhagic stroke patients, it was 19.4 ± 7.1 µmol/L. The difference was statistically significant (p = 0.88). The mean vitamin B12 level in ischemic stroke patients was 311.8 ± 128.3 pg/mL, compared to 372.9 ± 152.4 pg/mL in hemorrhagic stroke patients. Although the mean level was higher in hemorrhagic stroke patients, the difference was not statistically significant (p = 0.24). The mean folic acid level in ischemic stroke patients was 9.0 ± 2.8 ng/mL, whereas in hemorrhagic stroke patients, it was 7.9 ± 2.7 ng/mL. The difference was not statistically significant (p = 0.33).

Table No 2 : Correlation Between NIHSS With Homocysteine , Vitamin B12 And Folic Acid Level In Cases

Correlations (Cases)		Homocysteine (umol/L)	Vit B12 (pg/mL)	Folic acid (ng/mL)
NIH Stroke Scale	Spearman correlation	0.592**	- 0.254*	-0.123
	P	<0.0001	0.026	0.287
	N	77	77	77
** Correlation is significant at the level 0.01 level (2 – tailed)				
* Correlation is significant at the level 0.05 level (2 – tailed)				

There was a significant positive correlation between the NIH Stroke Scale and homocysteine levels (Spearman correlation = 0.592, p < 0.0001). There was a significant negative correlation between the NIH Stroke Scale and vitamin B12 levels (Spearman correlation = -0.254, p = 0.026). There was no significant correlation between the NIH Stroke Scale and folic acid levels (Spearman correlation = -0.123, p = 0.287).

DISCUSSION:

Monitoring homocysteine, vitamin B12, and folic acid levels can aid in identifying patients at higher risk for severe strokes, enabling healthcare providers to implement early and targeted nutritional interventions. This approach not only has the potential to reduce stroke incidence but also to mitigate the severity and improve outcomes for those who experience a stroke. The present study investigated the correlation between homocysteine, vitamin B12, and folic acid levels with stroke severity in acute stroke patients compared to healthy controls. Our findings reveal significantly elevated homocysteine levels and reduced vitamin B12 levels were associated with more severe strokes.

CONCLUSION :

A significant positive correlation was found between homocysteine levels and NIHSS scores suggesting that higher homocysteine levels were linked to increased stroke severity. Elevated homocysteine levels are a known risk factor for stroke, and our findings confirm their association with more severe strokes. Addressing vitamin B12 deficiency through dietary interventions or supplementation could be an important strategy in reducing stroke risk and severity. Folic acid alone did not show a significant impact on stroke severity, its combined deficiency with vitamin B12 can exacerbate hyperhomocysteinemia, further increasing stroke risk. In conclusion, the study highlights the importance of monitoring and managing homocysteine and vitamin B12 levels in stroke patients to reduce stroke severity and improve outcomes.

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