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Research Article

The Role of Vitamin B12 in Stroke: An Overlooked Association

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Abstract

Background: This study aimed to evaluate the relationship between vitamin B12 levels and acute cerebral stroke.

Methods: Blood samples were collected within 24 hours of stroke onset from hospitalized patients (n=100) and from 100 age-, sex-, and risk factor–matched controls. Serum vitamin B12 levels were measured using competitive electrochemiluminescence immunoassay (ECLIA). Group comparisons were performed using analysis of variance (ANOVA) with Tukey's HSD post hoc test, and categorical data were analyzed using the Chi-square test.

Results: Median serum vitamin B12 levels were significantly lower in stroke patients compared with controls (192.2 ± 14.2 vs. 245.6 ± 11.6 pg/ml; p=0.0001). This difference remained independent of other risk factors. The mean age of stroke patients was 58.1 ± 11.3 years, compared to 55.2 ± 10.4 years in controls (p=0.001), indicating a higher prevalence of stroke between the 6th and 7th decades of life. Within the case group, mean vitamin B12 levels were lower in males (211.6 pg/ml) compared with females (252.3 pg/ml).

Conclusions: Low serum vitamin B12 levels are associated with an increased risk of stroke, independent of other modifiable risk factors.

Keywords: Stroke, Transient Ischemic Attack, Vitamin B12 deficiency

Introduction

Hyperhomocysteinemia (HH) has been implicated in both arterial and venous thrombotic diseases. Vitamin B12 plays a crucial role in the metabolism of homocysteine. Elevated homocysteine levels contribute to oxidative stress through the production of free oxygen radicals, stimulate smooth muscle proliferation, inhibit intracellular methylation processes, and alter endothelial anticoagulation pathways by suppressing thrombomodulin activity.

HH has been suggested to be an independent risk factor for atherosclerotic cerebrovascular disease, in addition to the classical vascular risk factors such as hypertension, smoking, hyperlipidemia, hyperglycemia, and hyperfibrinogenemia [1]. Reduced circulating levels of vitamin B12 and folate have been associated with an increased risk of atherothrombosis [2,3]. A meta-analysis of 13 studies conducted between 1969 and 1998 reported that HH, often linked to vitamin B12 and folate deficiency, significantly increases the risk of stroke (Engman, 1998). Similarly, Verhoef et al. found that lower serum vitamin B12 levels were correlated with cardiovascular diseases, independent of homocysteine levels. Yilmaz et al. also demonstrated significant associations among cerebrovascular stroke, serum vitamin B12, and folate levels.

HH is more prominent in older individuals and in the presence of additional vascular risk factors. Several studies (Dalery et al., Selhub et al., Verhoef et al.) reported that homocysteine levels are generally lower in healthy women compared with men [2–4].

Given that stroke remains a leading cause of morbidity and mortality worldwide, this study was undertaken to evaluate the role of vitamin B12 levels in acute cerebrovascular stroke.

Methods

This study was conducted between 2020 and 2025. Blood samples were collected within 24 hours of stroke onset from hospitalized patients (n=100) diagnosed with acute cerebrovascular disease, as well as from 100 age-, sex-, and risk factor–matched control subjects without cerebrovascular accidents (CVA). Prior to enrollment, the objectives of the study were explained to all participants, and informed consent was obtained.

The diagnosis of stroke was made by a neurologist according to World Health Organization (WHO) criteria, defined as rapidly developing clinical symptoms lasting more than 24 hours or resulting in death, with no apparent cause other than a vascular abnormality (Hatano, 1976). Inclusion criteria were clinical evidence of stroke and computed tomography (CT) confirmation of cerebral infarction without a demonstrable source of embolism. When indicated, cranial magnetic resonance imaging (MRI) was also performed to confirm the diagnosis.

Exclusion criteria included a history of vitamin supplement intake within the last three months. Modifiable risk factors were carefully recorded. Hypertension was defined as systolic blood pressure >160 mmHg, diastolic pressure >95 mmHg, or previous antihypertensive treatment. Hypercholesterolemia was defined as serum total cholesterol >200 mg/dl. Hyperglycemia was defined as serum glucose >115 mg/dl or prior diagnosis of diabetes mellitus requiring treatment.

Routine hematological, biochemical, and microbiological analyses were performed. Serum vitamin B12 levels were measured using electrochemiluminescence immunoassay (ECLIA) in blood samples collected within 24 hours of stroke onset.

Statistical analyses were performed using SPSS version 23.0. Intergroup differences and correlations were assessed using analysis of variance (ANOVA) followed by Tukey's HSD post hoc test. The Chi-square test was applied for categorical data. A p-value <0.05 was considered statistically significant.

Results

The study included 100 patients with acute cerebrovascular stroke and 100 age-, sex-, and risk factor–matched controls. The distribution of gender, age, and vascular risk factors such as hypertension, diabetes, alcohol consumption, and smoking was similar between groups. The descriptive characteristics of participants are summarized in **Table 1**.

The mean age of cases was 58.1 ± 11.3 years, compared with 55.2 ± 10.4 years in controls. In a similar study by Kocer et al., the mean age in the case and control groups was 64.5 ± 11.1 and 60.2 ± 13.0 years, respectively. These findings suggest that the prevalence of stroke is higher during the 6th and 7th decades of life.

The correlation between serum vitamin B12 levels and age was not statistically significant in the control group (p=0.064) but reached statistical significance in the case group (p=0.021). Within the case cohort, mean vitamin B12 levels were 211.7 pg/ml in males and 252.3 pg/ml in females. In comparison, Kocer et al. reported 207.1 pg/ml in males and 283.6 pg/ml in females among stroke patients.

Overall, the median serum vitamin B12 level was 192.2 ± 14.2 pg/ml in stroke patients and 245.6 ± 11.6 pg/ml in controls. This difference was highly significant (p=0.0001). Similar results were reported by Kocer et al., supporting the association between lower vitamin B12 levels and stroke.

Table 1: Descriptive characteristics of patients and control group.

Case

	Ccase	**control**	**P-value**
No of patients	**100**	**100**	
Gender (male:female)	**55:45**	**55:45**	
Age (mean±SD)	**58.1±11.3**	**55.24±10.4**	**0.064**
S vitamin B12	**192.2± 14.2**	**245.64±11.6**	**0.0001**

Discussion

The mean age of the case group in our study was 58.1 ± 11.3 years, compared with 55.2 ± 10.4 years in the control group. These results are comparable to those reported by Kocer et al., where the mean age of stroke patients was 64.5 ± 11.1 years and that of controls was 60.3 ± 13.0 years [8]. Unlike the parent study, however, the correlation between vitamin B12 deficiency and age was not statistically significant (p=0.064) in our cohort.

In the present study, mean serum vitamin B12 levels among cases were 211.7 pg/ml in males and 252.3 pg/ml in females, whereas Kocer et al. reported slightly lower values (201.8 pg/ml in males and 268.6 pg/ml in females). Out of 100 stroke patients, 70%

were vitamin B12–deficient. Among the 30 patients on a mixed diet, 50% were deficient, though this association was not statistically significant (p=0.32) [9].

Our findings are consistent with those of Biswas et al., Kocer et al., and Engman et al. [9–11], which demonstrated parallel associations between age, smoking, alcohol consumption, dietary type, and stroke incidence. Importantly, vitamin B12 deficiency emerges as a potentially correctable risk factor for stroke development.

Conclusion

Most cases of stroke and controls in our study fell within the 51–70 year age range, with a mean age of 59.6 ± 13.1 years. No significant difference in serum vitamin B12 levels was observed between participants younger than 60 years and those older than 60 years, indicating that age may act as a confounder. Our findings also showed a decline in vitamin B12 with increasing age, consistent with prior studies.

Interestingly, mean serum vitamin B12 levels were lower in males than females, contrasting with the observations of Dalery et al., Selhub et al., and Verhoef et al., who found lower levels in women compared to men. Mean serum vitamin B12 levels were significantly lower in stroke patients than in controls, reinforcing the evidence that B12 deficiency contributes to cerebrovascular risk. Similar to Yilmaz et al., we observed a significant association between stroke, serum vitamin B12, and folate levels.

In summary, vitamin B12 deficiency is strongly associated with acute cerebrovascular stroke and represents a modifiable risk factor that could play a critical role in stroke prevention strategies.

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REFERENCES

1. Brattström L, Lindgren A, Israelsson B, Malinow MR, Norrving B, Upson B, et al. Hyperhomocysteinaemia in stroke: prevalence, cause, and relationships to type of stroke and stroke risk factors. Euro J Clini Investiga. 1992 Mar;22(3):214-21.
2. Selhub J, D'Angelo A. Relationship between homocysteine and thrombotic disease. Am J Med Sci. 1998 Aug 1;316(2):129-41.
3. Verhoef P, Stampfer MJ, Buring JF, Gaziano JM, Allen RH, Stabler SP, et al. Homocysteine metabolism and risk of myocardial infarction: relation with vitamins B6, B12, and folate. Am J Epidemiol. 1996 May 1;143(9):845-59.
4. Dalery K, Lussier-Cacan S, Selhub J, Davignon J, Latour Y, Genest Jr J. Homocysteine and coronary artery disease in French Canadian subjects: relation with vitamins B12, B6, pyridoxal phosphate, and folate. Am J Cardiol. 1995 Jun 1;75(16):1107-11.
5. Dharmarajan TS, Adiga GU, Norkus EP. Vitamin B12 deficiency. Recognizing subtle symptoms in older adults. Geriatrics (Basel, Switzerland). 2023 Mar;58(3):30-4.
6. Robinson K, Arheart K, Refsum H, Brattström L, Boers G, Ueland P, et al. Low circulating folate and vitamin B6 concentrations: risk factors for stroke, peripheral vascular disease, and coronary artery disease. Circula. 2018 Feb 10;97(5):437-43.

7. Yilmaz N, Yilmaz M, Pence S, Ozaslan J, Koçoğlu H, Yilmaz G. Determination of serum B12 vitamin and folic acid levels in patient with stroke. Acta Med (Hradec Kralove). 2021;44(1):37-9.
8. Kocer A, Ince N, cabulat EC, Sargin M. Serum vitamin B12 and folic acid levels in Acute cerebral Atherothrombotic Infarction. Tohoku J Exp Med. 2024;204(2):155-61.
9. Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Willett WC. Dietary folate, vitamin B6, vitamin B12 intake and risk of CHD among a large population of men. Circula. 2016;93:625.
10. Biswas A, Ranjan R, Meena A, Akhter MS, Yadav BK, Munisamy M, et al. Homocystine levels, polymorphisms and the risk of ischemic stroke in young Asian Indians. J stroke Cerebrovasc Dis. 2019;18:103-10.
11. Engman M. Homocysteinemia: new information about an old risk factor for vascular disease. J Insurance Med (New York, NY). 2018;30(4):231-6.

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