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The Role of Vitamin B12 Deficiency in Ischemic Stroke Risk and Outcome: A Prospective Observational Study

Dr. Sajid Baksh,Dr.Prashant Punekar[2] ,Dr.Anumiti Jain[3], Dr.Amit Pandey[4]
[1] *Junior Resident, Department Of Medicine, N.S.C.B. Jabalpur, Madhya Pradesh*
[2] *Associate Professor, Department Of Medicine, N.S.C.B. Jabalpur, Madhya Pradesh*
[3]*associate Professor, Department Of Neurology , N.S.C.B. Jabalpur, Madhya Pradesh*
[4]*junior Resident, Department Of Medicine, N.S.C.B. Jabalpur, Madhya Pradesh*

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ABSTRACT

Background: Ischaemic stroke is the most common cerebrovascular disease and is one of the leading causes of death and long-term disability in the world. Vitamin B12 deficiency, by virtue of causing hyperhomocysteinemia may be implicated as an acquired risk factor of ischaemic stroke, which is also easily modifiable. There is a lack of data from India regarding the prevalence of B12 deficiency and hence the correlation with ischaemic stroke patients. The objective of this study was to evaluate the role of vitamin B12 deficiency in ischemic stroke risk and outcome**.**

Material and methods :A prospective observational case-control study was conducted in the Department of General Medicine and Neurology at Netaji Subhash Chandra Bose Medical College & Hospital, Jabalpur, Madhya Pradesh, India, from July 2022 to January 2024. The study included 89 cases of acute ischemic stroke and 89 age- and sex-matched healthy controls. Data were collected using structured forms and analyzed using SPSS. Categorical variables were represented as frequency and percentage, while continuous variables were represented as mean and standard deviation. Chi-square test were used for statistical analysis. A p-value of <0.05 was considered significant.

Results: In the study population, Vitamin B12 deficiency is notably more prevalent among the cases than the controls. Specifically, 51.6% of the cases have low Vitamin B12 levels (<200 pg/ml), compared to only 7.9% of the controls. Conversely, 48.4% of the cases have normal Vitamin B12 levels (200-900 pg/ml), whereas a substantial 92.1% of the controls fall within the normal range. The chi-square statistic for this comparison is 40.86, with a p-value of less than .0001, indicating that the observed difference in Vitamin B12 levels between the cases and controls is highly statistically significant. This suggests a strong association between low Vitamin B12 levels and the condition being studied among the cases.

Conclusions: Vitamin B12 deficiency appear to be important risk factors for cerebrovascular accidents. It is therefore important to assess vitamin B12 levels in all cases of cerebrovascular accidents.

I. INTRODUCTION

The World Health Organization (WHO) defines stroke as an event caused by the interruption of blood supply to the brain, typically due to a burst or blocked blood vessel [1]. Stroke, the most common clinical manifestation of cerebrovascular disease, is a significant endpoint of atherosclerosis, impacting the cerebral blood vessels that supply the brain. It is a major global health issue, ranking as the second leading cause of mortality and the fourth leading cause of disability worldwide. In ischemic strokes, atherosclerosis, a chronic inflammatory condition where immune mechanisms interact with nutrition, plays a central role and is a modifiable risk factor for stroke [2].

Vitamin B12 deficiency, particularly in late adulthood, is linked to an increased risk of ischemic stroke. This deficiency elevates homocysteine levels, a recognized risk factor for ischemic stroke. Additionally, changes in myelination due to vitamin B12 deficiency may further contribute to neurological dysfunction and an increased stroke risk [3].

This study aims to investigate the correlation of vitamin B12 levels with the severity and prognosis of patients with ischemic stroke.

II. METHODOLOGY:

Study Design and Setting

A prospective observational case-control study was conducted in the Department of General Medicine and Neurology at Netaji Subhash Chandra Bose Medical College & Hospital, Jabalpur, Madhya Pradesh, India, from July 2022 to January 2024.

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Sample Size

The study included 89 cases of acute ischemic stroke and 89 age- and sex-matched healthy controls.

Inclusion Criteria

- Patients ≥16 years with acute ischemic stroke.
- Confirmed ischemic stroke by imaging.
- Written consent.

Exclusion Criteria

- Age <16 years.
- Transient Ischemic Attack (TIA).
- Recurrent cerebrovascular accidents.
- Hemorrhagic strokes.
- Head trauma or neuroinfection.
- Recent vitamin B12 supplementation.

Data Collection and Analysis

Data were collected using structured forms and analyzed using SPSS. Categorical variables were represented as frequency and percentage, while continuous variables were represented as mean and standard deviation. Chi-square test were used for statistical analysis. A p-value of <0.05 was considered significant.

Ethical Consideration

Ethical approval was obtained before the commencement of study of institutional ethical committee.

III. RESULTS:

The age group of 46-60 years had the highest percentage of both cases (41.7%) and controls (40.4%), indicating a significant representation of this age group in the study population.

A predominant male population was observed in both groups, with 73% of cases and 71% of controls being male.(table 1)

Table 1:
Distribution of Study Participants by Demographic Characteristics and Sex

Characteristics	**Cases N (%)**	**Controls N (%)**
Demographic (**Age Group**)		
16-30	9 (10.1)	5 (5.6)
31-45	23 (25.8)	26 (29.2)
46-60	37 (41.7)	36 (40.4)
>60	20 (22.4)	22 (24.8)
Total	89 (100)	89 (100)
Sex		
Male	65 (73)	63 (71)
Female	24 (27)	26 (29)
Total	89 (100)	89 (100)

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Table 2: Distribution of Study Participants by Risk Factors, Addiction History and Vitamin B12 Levels

Risk Factors	Cases N (%)	Controls N (%)	p-value
Hypertension	51 (57.3)	21 (23.6)	0.00001
Diabetes Mellitus	20 (22.5)	8 (9.0)	0.0136
Coronary Artery Disease	17 (19.1)	2 (2.2)	0.0002
BMI (Overweight)	58 (65.2)	24 (27.0)	0.0001
Addiction History			
Alcohol	18 (20.2)	9 (10.1)	0.05
Smoking	38 (42.7)	25 (28.1)	0.03
Vitamin B12 (pg/ml)			
Low (<200)	46 (51.6)	7 (7.9)	<0.0001
Normal (200-900)	43 (48.4)	82 (92.1)	
Total	89 (100)	89 (100)	

Table 3: Severity and Outcome of Stroke in Relation to Vitamin B12 Levels

NIHSS Severity Score	Cases N (%)	Low B12 N (%)	Normal B12 N (%)	
Minor (1-4)	20 (22.5)	7 (15.2)	13 (30.2)	**p-value** 0.68
Moderate (5-15)	48 (53.9)	25 (54.3)	23 (53.5)	
Moderate-Severe (16-20)	4 (4.5)	2 (4.3)	2 (4.7)	
Severe (21-42)	17 (19.1)	12 (26.2)	5 (11.6)	
Vitamin B12 Levels	**Discharge N (%)**	**Death N (%)**	**Total**	
Low	36	10	46	
Normal	39	4	43	
Total	75	14	89	
p-value	**0.10732**			

Risk Factors- Hypertension, diabetes mellitus, and coronary artery disease were significantly more prevalent in stroke cases compared to controls, highlighting these conditions as major risk factors.(table 2)

Addiction History- Higher proportions of alcohol consumption and smoking were observed among stroke cases compared to controls.(table 2)

Vitamin B12 (pg/ml) Level-Vitamin B12 deficiency was significantly more prevalent among stroke cases (51.6%) compared to controls (7.9%).(table 2)

Severity- No significant association was found between Vitamin B12 levels and stroke severity, though severe cases had a higher proportion of low B12 levels.(table 3)

Outcome-Patients with normal Vitamin B12 levels had a better prognosis, with higher discharge rates and lower mortality compared to those with low Vitamin B12 levels, though the difference was not statistically significant.

IV. DISCUSSION

The study revealed a significant association between low Vitamin B12 levels and the occurrence of ischemic stroke, with 51.6% of stroke cases showing Vitamin B12 deficiency compared to only 7.9% of controls. This aligns with previous studies indicating that Vitamin B12 deficiency elevates homocysteine levels, increasing the risk of cerebrovascular diseases [3].

Risk factors such as hypertension, diabetes, and coronary artery disease were significantly more prevalent in stroke cases. This finding is consistent with Kernan et al. (2014), who identified hypertension as responsible for up to 50% of stroke cases [4]. Similarly, Feigin et al. (2014) noted that diabetes mellitus increases stroke

factor, with a higher mean BMI observed in stroke cases compared to controls. This finding underscores the importance of weight management in stroke prevention [4].

Higher proportions of alcohol consumption and smoking were observed among stroke cases. This is consistent with existing literature that identifies smoking as a major risk factor for stroke due to its role in promoting atherosclerosis and increasing blood clot formation [4].

The severity of stroke, measured by NIHSS score, showed varying proportions of low and normal Vitamin B12 levels across different severity categories. However, the association was not statistically significant, suggesting that while Vitamin B12 deficiency is associated with stroke occurrence, it may not directly influence stroke severity.

Patients with normal Vitamin B12 levels had a better prognosis, with a higher discharge rate and lower mortality compared to those with low Vitamin B12 levels. This finding is supported by previous research, which highlights the beneficial effects of maintaining adequate Vitamin B12 levels on stroke outcomes [6].

Overall, this study underscores the significant role of Vitamin B12 deficiency in the occurrence of ischemic stroke and the importance of addressing this modifiable risk factor in stroke prevention and management strategies. Regular screening and supplementation of Vitamin B12, particularly in high-risk populations, along with the management of other risk factors, are crucial steps in reducing the incidence and improving outcomes of ischemic stroke

Conflict of Interest The authors declare no conflict of interest.

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V. LIMITATIONS

The study's limitations include a limited sample size, cross-sectional design limiting causality establishment, potential confounding risk by 1.5 to 3 times due to hyperglycemiainduced vascular damage [5].

The study highlights the critical need for managing these modifiable risk factors through lifestyle changes and medical interventions. Obesity was also found to be a significant risk

factors like diet and lifestyle not fully controlled, and the study population may not represent the broader population.

VI. RECOMMENDATIONS

Promoting dietary guidelines that include Vitamin B12-rich foods and developing guidelines for Vitamin B12 supplementation, especially for high-risk individuals, is essential. Implementing routine Vitamin B12 level screening for at-risk populations and targeting high-risk groups like vegetarians and the elderly for frequent monitoring is recommended. Public health interventions should include awareness campaigns on the role of Vitamin B12 in preventing ischemic stroke and integrating Vitamin B12 education and screening into community health programs. Clinically, reinforcing blood pressure monitoring and management, stringent glycemic control, comprehensive CAD screening, and weight management programs should be prioritized. Behavioral interventions such as smoking cessation and responsible alcohol consumption guidelines are also crucial. Further longitudinal studies are needed to explore the relationship between Vitamin B12 levels and stroke outcomes in more detail.

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