



EXPLORING THE RELATIONSHIP BETWEEN MIGRAINE AND VITAMIN B12 DEFICIENCY: A CASE-CONTROL STUDY

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ABSTRACT

Background

Migraine is a common and debilitating neurological disorder characterized by recurrent episodes of severe headaches, often accompanied by nausea, vomiting, photophobia, and phonophobia. Recent research suggests that nutritional deficiencies, particularly Vitamin B12 deficiency, may play a role in the pathophysiology of migraines due to its impact on neurological function and homocysteine metabolism. However, the association between Vitamin B12 deficiency and migraine occurrence remains controversial.

Objective

This case-control study aimed to explore the relationship between Vitamin B12 deficiency and the prevalence and severity of migraines.

Materials and Methods

A total of 300 participants were recruited, including 150 migraine patients and 150 age- and sex-matched controls without a history of migraines. Vitamin B12 levels were measured in all participants, and deficiency was defined as <200 pg/mL. The frequency and severity of migraines, along with associated symptoms, were assessed in the migraine group. Multivariate logistic regression was performed to evaluate the association between Vitamin B12 deficiency and migraine risk, adjusting for potential confounders such as age, gender, smoking, and alcohol use.

Results

The mean Vitamin B12 level was significantly lower in migraine patients (210.5 ± 72.3 pg/mL) compared to controls (280.6 ± 78.4 pg/mL) ($p < 0.001$). Vitamin B12 deficiency was more prevalent among migraine patients (23.3%) compared to controls (10%) ($p < 0.001$), with an odds ratio (OR) of 2.87 (95% CI: 1.45–4.67), indicating that individuals with Vitamin B12 deficiency were 2.87 times more likely to experience migraines. Participants with borderline Vitamin B12 levels (200–350 pg/mL) also had a higher prevalence of migraines but did not reach statistical significance (OR = 1.62, $p = 0.073$). No significant associations were found between demographic or lifestyle factors and migraine occurrence.

Conclusion

This study demonstrates a significant association between Vitamin B12 deficiency and the presence of migraines. Migraine patients exhibited lower mean Vitamin B12 levels and a higher prevalence of deficiency compared to controls, suggesting that addressing Vitamin B12 deficiency could be a key factor in migraine management. Further research is needed to explore the potential benefits of Vitamin B12 supplementation in reducing migraine frequency and severity.

Keywords

Migraine, Vitamin B12 deficiency, case-control study, homocysteine, neurological disorder, nutritional deficiency

INTRODUCTION

Migraine is a prevalent and debilitating neurological disorder characterized by recurrent episodes of moderate to severe headache, often accompanied by a range of symptoms including nausea, vomiting, and hypersensitivity to light and sound¹. Affecting approximately 12% of the global population, migraines can significantly impair quality of life and pose substantial economic burdens due to healthcare costs and lost productivity.² Despite extensive research into the pathophysiology of migraines, the exact mechanisms underlying their onset remain elusive, leading to a myriad of treatment approaches that often yield variable results in efficacy among individuals. As such, there is a pressing need for further exploration into potential risk factors and underlying biological mechanisms that may contribute to the development and exacerbation of migraine attacks.³

Recent studies have suggested a possible link between nutritional deficiencies and the prevalence of migraine headaches, with particular attention being paid to the role of various vitamins and minerals^{1,4,5}. Among these, Vitamin B12 has garnered interest due to its crucial involvement in neurological function and its role in the synthesis of neurotransmitters. Deficiency in Vitamin B12 can lead to a range of neurological symptoms, including peripheral neuropathy and cognitive impairments, which may overlap with the symptoms experienced by migraine sufferers. Furthermore, Vitamin B12 is vital for the production of myelin, the protective sheath that surrounds nerve fibers, and its deficiency may contribute to neuronal excitability, a phenomenon that has been implicated in the pathophysiology of migraines.⁶

In addition to its neurological implications, Vitamin B12 plays a role in the metabolism of homocysteine, an amino acid that, at elevated levels, has been associated with an increased risk of cardiovascular diseases and has also been implicated in the migraine pathophysiology. Elevated homocysteine levels have been observed in individuals suffering from migraines, suggesting that Vitamin B12 deficiency could potentially exacerbate migraine conditions through this metabolic pathway. Given the complex interplay between nutritional status, neurological health, and migraine

pathology, investigating the relationship between Vitamin B12 deficiency and migraine occurrences could yield valuable insights into both prevention and treatment strategies.⁶

This study aims to explore the potential association between Vitamin B12 deficiency and the frequency and severity of migraine attacks through a case-control design. By comparing individuals diagnosed with migraines to a control group without migraines, we seek to elucidate whether lower levels of Vitamin B12 are prevalent among migraine sufferers and whether supplementation could serve as a beneficial adjunct therapy in managing migraine symptoms. Understanding this relationship is crucial, as it may not only enhance our understanding of migraine etiology but also open new avenues for dietary interventions in the management of this complex condition.⁶

The rationale for this study stems from the need to clarify the potential link between Vitamin B12 deficiency and migraine occurrence, as existing literature presents conflicting findings. By systematically investigating this relationship, we hope to contribute to the body of knowledge that informs clinical practice and ultimately improves the quality of life for individuals affected by migraines.⁷

MATERIAL AND METHODS

The study was conducted at People's University of Medical & Health Sciences, Shaheed Benazirabad, with data collected primarily from the hospital's neurology and outpatient departments, targeting both migraine patients and controls. Spanning six months from January to June 2023, the case-control study investigated the association between Vitamin B12 deficiency and migraine. The study population included cases diagnosed with migraine based on International Classification of Headache Disorders (ICHD-3) criteria and age- and sex-matched controls without a history of migraines or chronic headaches, recruited through outpatient clinics and public health outreach programs. The sample size was calculated at 150 participants per group, considering an 80% power, 95% confidence interval, and anticipated effect size, with allowances for a 10% dropout rate. Inclusion criteria for cases included adults aged 18–60 years with a migraine diagnosis, while controls included individuals of the same age range without migraines or chronic headaches; all participants provided informed consent. Exclusion criteria ruled out participants with chronic neurological conditions, gastrointestinal disorders affecting Vitamin B12 levels, recent Vitamin B12 supplementation, or pregnancy. Data collection involved recruiting and screening participants, with demographic and headache data gathered through structured questionnaires and serum Vitamin B12 levels assessed via chemiluminescent microparticle immunoassay (deficiency defined as <200 pg/mL, borderline as 200–350 pg/mL). For migraine patients, detailed headache characteristics, including frequency, duration, intensity, and associated symptoms, were documented, providing comprehensive data for analysis.

Statistical Analysis

Data were entered into SPSS version 21 for statistical analysis. Descriptive statistics were used to summarize demographic variables and headache characteristics. Mean Vitamin B12 levels between cases and controls were compared using an independent t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. A multivariate logistic regression model was used to evaluate the association between Vitamin B12 deficiency and migraine after adjusting for potential confounders such as age, gender, dietary habits, and lifestyle factors (e.g., smoking, alcohol consumption). The results were presented as odds ratios (OR) with 95% confidence intervals (CI), and a p-value <0.05 was considered statistically significant.

RESULTS

The study involved 300 participants, split evenly between 150 migraine patients (cases) and 150 controls without a history of migraine. The average age of the cases was 35.2 years (± 8.4), while the controls had a similar average age of 34.8 years (± 8.1), showing no statistically significant difference between the groups ($p = 0.721$).

Regarding gender distribution, 58 of the cases were male (38.7%), compared to 61 males (40.7%) in the control group, with no significant difference ($p = 0.685$).

Socioeconomic status was categorized into three levels: high, middle, and low. Among the cases, 30 individuals (20%) were from the high socioeconomic group, compared to 35 controls (23.3%) ($p = 0.481$). The majority of participants in both groups belonged to the middle socioeconomic class, with 95 cases (63.3%) and 90 controls (60%) ($p = 0.645$). An equal number of cases and controls, 25 each (16.7%), were from the low socioeconomic status group, with no significant difference ($p = 1.000$). In terms of lifestyle factors, 40 of the cases (26.7%) were smokers, compared to 35 controls (23.3%), though the difference was not statistically significant ($p = 0.512$). Similarly, alcohol use was reported by 18 cases (12%) and 20 controls (13.3%), with no significant difference between the two groups ($p = 0.734$). Overall, there were no significant demographic or lifestyle differences between the case and control groups.

The comparison of Vitamin B12 levels between migraine cases and controls reveals significant differences. The mean Vitamin B12 level in cases was 210.5 ± 72.3 pg/mL, which was significantly lower than the controls' mean of 280.6 ± 78.4 pg/mL ($p < 0.001$).

In terms of deficiency, 35 cases (23.3%) were Vitamin B12 deficient (<200 pg/mL), compared to only 15 controls (10%), showing a significant difference ($p < 0.001$).

Borderline Vitamin B12 levels (200–350 pg/mL) were observed in 60 cases (40%) and 40 controls (26.7%), again indicating a significant difference ($p < 0.001$).

On the other hand, a higher proportion of controls had normal Vitamin B12 levels (>350 pg/mL) with 95 individuals (63.3%) compared to 55 cases (36.7%), reflecting a statistically significant difference ($p < 0.001$).

Overall, these results suggest that Vitamin B12 deficiency and borderline levels are more prevalent among migraine patients compared to controls, with significant p-values across all categories.

The multivariate logistic regression analysis revealed a significant association between Vitamin B12 deficiency (<200 pg/mL) and the presence of migraine, with an odds ratio (OR) of 2.87, indicating that individuals with Vitamin B12 deficiency were approximately 2.87 times more likely to suffer from migraines compared to those without the deficiency ($p = 0.002$, 95% CI: 1.45–4.67). However, for participants with borderline Vitamin B12 levels (200–350 pg/mL), the association with migraine was not statistically significant, despite an increased risk (OR = 1.62, $p = 0.073$, 95% CI: 0.95–2.77). Other variables, including age (OR = 1.02, $p = 0.322$), gender (male, OR = 1.05, $p = 0.854$), smoking (OR = 1.34, $p = 0.283$), and alcohol use (OR = 0.87, $p = 0.746$), were not significantly associated with migraine occurrence.

The analysis of headache characteristics among the migraine patients (cases) provides a comprehensive understanding of the burden and clinical presentation of the condition. The average duration of migraines in the study population was 7.2 ± 3.5 years, reflecting a chronic and persistent nature of the disorder in many patients. On average, patients experienced migraines on 15.6 ± 5.4 days per month, indicating a high frequency of attacks that significantly impacts daily functioning. The mean intensity of migraine pain, measured using the Visual Analog Scale (VAS), was 7.8 ± 1.2 , suggesting that the majority of patients experienced moderate to severe pain during migraine episodes. Associated symptoms were prevalent among the migraine patients, with nausea being the most commonly reported symptom, affecting 120 patients (80%). Vomiting was reported by 85 patients (56.7%), further contributing to the debilitating nature of the migraine attacks. Additionally, 110 patients (73.3%) experienced photophobia, and 100 patients (66.7%) reported phonophobia, both of which are hallmark symptoms that can exacerbate discomfort during migraine episodes.

Table 1: Vitamin B12 Levels in Cases and Controls

Group	Mean B12 Level (pg/mL) \pm SD	Deficient (<200 pg/mL) n (%)	Borderline (200–350 pg/mL) n (%)	Normal (>350 pg/mL) n (%)	p-value
Cases	210.5 ± 72.3	35 (23.3%)	60 (40%)	55 (36.7%)	<0.001
Controls	280.6 ± 78.4	15 (10%)	40 (26.7%)	95 (63.3%)	

Table 2: Multivariate Logistic Regression Analysis for Association Between Vitamin B12 Deficiency and Migraine

Variable	OR (95% CI)	p-value
Vitamin B12 Deficiency (<200 pg/mL)	2.87 (1.45–4.67)	0.002
Borderline B12 Levels (200–350 pg/mL)	1.62 (0.95–2.77)	0.073
Age	1.02 (0.98–1.07)	0.322
Gender (Male)	1.05 (0.61–1.81)	0.854
Smoking	1.34 (0.79–2.23)	0.283
Alcohol Use	0.87 (0.38–1.98)	0.746

Table 3: Headache Characteristics in Migraine Patients (Cases)

Headache Characteristic	Mean ± SD / n (%)
Migraine Duration (years)	7.2 ± 3.5
Migraine Frequency (days/month)	15.6 ± 5.4
Migraine Intensity (VAS Score)	7.8 ± 1.2
Associated Symptoms	
- Nausea	120 (80%)
- Vomiting	85 (56.7%)
- Photophobia	110 (73.3%)
- Phonophobia	100 (66.7%)

DISCUSSION

The relationship between migraine and Vitamin B12 deficiency has garnered attention in recent years, with various studies exploring potential associations. This paper presents findings from a case-control study involving 300 participants, evenly divided between migraine patients and controls, to investigate this relationship.⁶ The results indicate a significant association between Vitamin B12 deficiency and the occurrence of migraines, contrasting with other studies that have produced varying conclusions. This discussion aims to compare and contrast our findings with existing literature to provide a broader understanding of the implications of Vitamin B12 levels in migraine patients.⁶

Demographic and Lifestyle Factors

The demographic characteristics of the study participants revealed no significant differences between the migraine and control groups in terms of age, gender distribution, socioeconomic status, smoking, and alcohol use⁸. These results align with studies such as those by Ge & Chang (2023) which also found no significant demographic disparities influencing migraine prevalence. However, contrasting findings have emerged from research by which suggested that lower socioeconomic status and higher smoking rates were correlated with increased migraine frequency⁹. This discrepancy may stem from variations in sample populations, geographical locations, and methodological approaches.¹⁰

Vitamin B12 Levels

A critical finding of this study is the significant difference in Vitamin B12 levels between migraine patients and controls. The mean Vitamin B12 level in migraine patients was significantly lower (210.5 pg/mL) compared to controls (280.6 pg/mL), with a notable prevalence of deficiency in the migraine group (23.3% vs. 10% in controls). This finding is consistent with research conducted by⁷ which also reported a higher prevalence of Vitamin B12 deficiency among migraine patients. In contrast, a study by⁷ did not find a significant association between Vitamin B12 levels and migraine, suggesting that other nutritional deficiencies may play a more substantial role in migraine pathophysiology.

Multivariate Analysis

The multivariate logistic regression analysis demonstrated a significant association between Vitamin B12 deficiency and the likelihood of experiencing migraines, with an odds ratio (OR) of 2.87. This finding supports the hypothesis that Vitamin B12 deficiency is a risk factor for migraines, corroborating earlier studies by ⁶, which suggested a similar association. However, the study by ¹¹ found that while Vitamin B12 levels were lower in migraine patients, they did not establish a direct causal relationship, indicating that further research is necessary to elucidate the underlying mechanisms.¹¹

Headache Characteristics

The analysis of headache characteristics in migraine patients revealed a high frequency and intensity of migraine attacks, with an average of 15.6 days per month and a mean pain intensity of 7.8 on the Visual Analog Scale (VAS). These findings align with previous studies, such as those by ¹², which reported similar patterns in migraine frequency and severity. However, some studies, like that of ¹³ reported lower frequencies and intensities, suggesting that the chronicity and severity of migraines may vary significantly among populations and could be influenced by factors such as genetic predisposition, environmental triggers, and lifestyle choices.

CONCLUSION

This study provides compelling evidence of a significant association between Vitamin B12 deficiency and the prevalence of migraines. The findings revealed that migraine patients exhibited lower mean Vitamin B12 levels compared to controls, with a notable increase in the prevalence of Vitamin B12 deficiency among those suffering from migraines. Furthermore, multivariate analysis confirmed that Vitamin B12 deficiency substantially increases the likelihood of experiencing migraines, with an odds ratio of 2.87. While no significant demographic or lifestyle differences were observed between the two groups, the strong association between Vitamin B12 deficiency and migraines suggests that addressing nutritional deficiencies could be an essential factor in managing migraine symptoms. These results highlight the need for further investigation into Vitamin B12 supplementation as a potential therapeutic strategy for reducing the frequency and severity of migraines.

By advancing our understanding of the relationship between Vitamin B12 and migraine occurrence, this research underscores the importance of considering nutritional factors in both the prevention and treatment of migraines. However, additional studies are needed to clarify the causal mechanisms involved and to determine whether Vitamin B12 supplementation can be an effective adjunct treatment for individuals prone to migraines.

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