



Original Research

Clinical Determinants and Neurological Manifestation Among Adult Patients with Vitamin B Deficiency

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ABSTRACT

Objective: To assess the factors and neurological manifestations in adult patients with vitamin B12 deficiency.

Materials & Methods: A cross-sectional study was carried out at the Department of Neurology, Liaquat University of Medical and Health Sciences (LUMHS) for the period of Six months after the approval of the study from March 7, 2023, to September 6, 2023. The sample size was calculated using the WHO sample calculator, a total of 253 patients were enrolled. The data was obtained from patients fulfilling the inclusion criteria, and complete history and investigations were done on all the included patients. The data was assessed using SPSS version 23.

Results: The study included 253 patients with a mean age of 46.9 ± 11.5 years, of which 68% were male and 32% were female. Various neurological manifestations were observed among patients with vitamin B12 deficiency. The most common symptom was nerve numbness, affecting 65.2% of patients, followed by motor weakness in 24.1%. Non-traumatic compressive myopathy was found in 20.5% of patients. Other symptoms included ataxia (18.2%), impaired position sensation (14.2%), impaired vibration sensation (11.1%), and optic atrophy (3.9%). Signs of dementia were noted in 4.7% of cases. These findings highlight the diverse range of neurological symptoms linked to vitamin B12 deficiency and their varying prevalence.

Conclusion: It is to be concluded that a wide spectrum of neurological symptoms is associated with vitamin B12 deficiency, highlighting its potential impact on neurological health. Nerve numbness stands out as the most prevalent symptom, affecting a significant majority of patients, followed by motor weakness and non-traumatic compressive myelopathy.

Keywords: Vitamin B, Deficiencies, Neurological issues, Clinical Determinants.

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INTRODUCTION

Vitamin B deficiency is a serious health issue, which can lead to hematological, Ophthalmic, and problems of psychiatrist and neurotypical symptoms.¹ Sub-acute combined "spinal cord degeneration" (SCD) is one of the major occurring problems due to vitamin B deficiency and SCD mainly alters the dorsal and lateral columns of the spinal cord.² The resultant neurological symptoms are paresthesia, ataxia, and weakness of the limbs. In developing and underdeveloped countries vitamin B12 deficiency is a common condition among the general population and seems to be proliferating,¹ with the older population being affected the most.³ Inadequate levels of vitamin B12 also have been associated with various clinical statuses and thus not individually related to a single symptom or cluster of symptoms.⁴ Comparative analysis of vitamin B12 levels in several selected groups reported that the cause of deficiency among the older population was due to hematologic or neurologic anomalies, however, gastrointestinal and possibly vascular symptoms were also common.⁵ The deficiency of vitamin B causes neurological impairments and disabilities throughout the world; however, the other diseases remain unchanged, the broad spectrum of pathological states of patients with vitamin B deficiency is also linked to the age of patients. Neurodegenerative disorders among older adults are more common around the world along with Alzheimer's, Parkinson's diseases vascular and temporal dementia, disabilities, and deaths. Dementia is a disease of raising concern and its high prevalence is an expected problem and increasing among the older population.⁶⁻⁷

According to the World Health Organization (WHO), 35.6 million people are suffering from dementia currently and the data might double up by the end of the year 2030 and three times by the end of 2050.⁸ Vitamin B deficiency is reportedly neurological causes the associated complications

if they are left untreated. Despite knowing the health-related concerns the unavailability of accurate data, and accurate numbers of patients increases the desire for more focused research and the need for more studies to assess the consequences of dealing with this ailment.⁹ This sort of study and research approach helps in assessing the health burden and understanding the need for more advancements among the populations which are ignored the majority of the time.¹⁰⁻¹²

The current study aimed to assess the neurological manifestation among patients with vitamin B deficiency. Furthermore, this study filled the gap opened a new forum of discussion, and provided knowledge and information regarding the medical workup of these patients. A continuous rise in the daily activities and optic atrophy and signs of dementia are observed more often among the population and they emphasize the critical importance of timely diagnosis and management of this deficiency to prevent severe neurological complications. These findings underscore the urgency of early detection and treatment of vitamin B12 deficiency to mitigate the risk of a broad range of neurological manifestations. Unfortunately, a country like Pakistan has limited resources for health care setups and providing quality of life to the population hence the current study aims to determine the frequency of neurological manifestation in patients with vitamin B12 deficiency visiting a tertiary care hospital.

PATIENTS AND METHODS

Study Design & Setting

A Descriptive Cross-Sectional Study was carried out at the Department of Neurology, LUMHS, Jamshoro. For the duration of 06 months from March 7, 2023, to September 6, 2022, after obtaining approval from the Research Evaluation Unit (CPSP/REU/NEU-2021-164-656).

Sampling

The sample size of 253 was calculated using the WHO sample calculator considering the frequency/prevalence of dementia¹³ i.e., 4.3% margin of error considered as 2.5% and confidence interval (CI) 95%.

Inclusion Criteria

Both genders age 40 years to 80 years with a confirmed diagnosis of vitamin B deficiency. Transient ischemic attack, Subarachnoid hemorrhage & venous sinus thrombosis (If focal neurological deficit (assessed clinically) resolves within 24 hours and no sign of infarct on CT and provide informed consent included in the study.

Exclusion Criteria

Patients with known psychiatric issues, inability to communicate, patients on antidepressants, and pregnant patients were excluded from the study.

Ethical Approval

Ethical approval is provided as per requirement from the Research Evaluation Unit (CPSP/REU/NEU-2021-164-656).

Data Collection & Clinical Management

The sampling technique used was the non-probability sampling technique. All patients who fulfilled the inclusion criteria and presented to the outpatient Department of Neurology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro with any neurological disorder fulfilled the inclusion criteria were included in the study after obtaining written informed consent from the patient or next of kin before inclusion after explaining the risk and benefit of the upcoming study. Complete history and investigations which include CBC, peripheral smear, stool d/r, bone marrow, and serum B12

were done on all the included patients. MRI of all the included patients was done. All the patients were assessed for neurological manifestation i.e. (non-traumatic compressive myelopathy, nerve numbness, optic atrophy, ataxia, dementia, impaired position sensation, impaired vibration sensation, and motor weakness) by the operational definition by the researcher himself under the supervision of consultant > 5 years of experience. Biasness was controlled by strictly following inclusion criteria.

Data Analysis

The collected data was analyzed by SPSS version 23. Descriptive statistics were calculated, and data was analyzed and generated with a 95% confidence Interval. Mean \pm SD / Median with IQR as appropriate was calculated for age and serum level. Frequencies and percentages were calculated for gender, residential status, employment status, and neurological manifestation i.e. non-traumatic compressive myelopathy, nerve numbness, optic atrophy, ataxia, dementia, impaired position sensation, impaired vibration sensation, and motor weakness. Data was stratified based on age, gender, residential status, and employment status to see the effect of these on outcome variables, and a chi-square test was applied. A *p*-value of less than 0.05 was considered clinically significant.

RESULTS

In this study, a total of 253 patients were enrolled for the neurological manifestation in patients with vitamin B12 deficiency visiting tertiary care hospital, of which 172 (68.0%) were male whereas, 81 (32.0%) were female with mean \pm SD of age was 46.9 \pm 11.5 years and mean \pm SD of serum level was 91.3 \pm 7.2 pmol/L as shown in Table 1.

Table 1: Descriptive statistics of Age and Serum levels of patients (n=253).

Variables	Mean± Standard Deviation
Age (Years)	46.9 ±11.5
Serum Levels (Pmol/L)	91.3±7.2
95% Confidence Interval	45.50 ±48.36
Minimum	40
Maximum	80
Range	40

Neurological Manifestation of Patients with Vitamin B deficiency

The Neurological manifestation showed non-traumatic compressive myopathy in 52 (20.5%) patients, nerve numbness was 165 (65.2%), optic atrophy in 10 (3.9%), and impaired position sensation in 36 (14.2%). Impaired vibration sensation 28 (11.1%), ataxia 46 (18.2%), dementia 12 (4.7%) and motor weakness were noted in 61 (24.1%) patients as mentioned in Table 2.

Stratification of Age Groups and Genders Concerning Neurological Manifestation

It compares the prevalence of conditions like non-traumatic compressive myelopathy, nerve numbness, and ataxia across two age groups (20–40 and >40 years) and genders (male and female). P-values are also provided to assess statistical significance. The data highlights differences in the

occurrence of neurological symptoms between age groups and genders, with nerve numbness being more common in younger age groups, particularly in males as mentioned in Table 3.

Table 2: Frequency of neurological manifestations in patients with vitamin B deficiency.

Neurological Manifestation	Frequency (n)	Percentage (%)
Non-Traumatic Compressive Myelopathy	52	20.5%
Nerve Numbness	165	65.2%
Optic Atrophy	10	3.9%
Impaired Position Sensation	36	14.2%
Impaired Vibration Sensation	28	11.1%
Ataxia	46	18.2%
Dementia	12	4.7%
Motor Weakness	61	24.1%

Stratification of Residential and Employment Status with Neurological Manifestation

In the distribution of residential status, 67 (26.5%) were urban residents while 186 (73.5%) patients were rural residents. Out of 253 patients, 161 (63.6%) were employed while 92 (36.4%) were unemployed Stratification of age group, gender, residential status, and employment status was done concerning neurological manifestation to assess significant differences.

Table 3: Results of the Chi-square test between the stratification of Age Groups and Genders concerning Neurological Manifestation (n=253).

Neurological manifestation	Age group [in years]		p-value	Gender		p-value
	20 – 40	>40		Male	Female	
Non-Traumatic Compressive Myelopathy	29(7.1%)	23 (5.6%)	0.722	35(9.0%)	17(4.4)	0.355
Nerve Numbness	104(25.4%)	61 (14.9%)		115(29%)	30(7.7%)	
Optic Atrophy	7(1.7%)	3 (0.7%)		6(1.5%)	4(1.0%)	
Impaired-Position Sensation	26(6.3%)	10 (2.4%)		25(6.4%)	11(2.8%)	
Impaired-Vibration Sensation	19(4.6%)	9(2.2%)		18(4.6%)	10(2.6%)	
Ataxia	30(7.3%)	16(3.9%)		31(7.9%)	15(3.8%)	
Dementia	8(2.0%)	4(1.0%)		8(2.1%)	4 (1.0%)	
Motor Weakness	34(8.3%)	27(6.6%)		40(10.3%)	21 (5.4%)	

Table 4: Results of the chi-square test between stratification of residential and employment status with neurological manifestations (n = 253).

Neurological manifestation	Residential status		p-value	Employment status		p-value
	Urban	Rural		Employed	Unemployed	
Non-Traumatic Compressive Myelopathy	12 (2.9%)	40(9.8%)	0.035	33(8.0%)	19(4.6%)	0.059
Nerve Numbness	49(12.0%)	116(28.3%)		130(31.7%)	35(8.5%)	
Optic Atrophy	2(0.5%)	8(2.0%)		5(1.2%)	5(1.2%)	
Impaired Position Sensation	20(4.9%)	16(3.9%)		24(5.9%)	12(2.9%)	
Impaired Vibration Sensation	11(2.7%)	17(4.1%)		18(4.4%)	10(2.4%)	
Ataxia	12(2.9%)	34(8.3%)		28(6.8%)	18(4.4%)	
Dementia	5(1.2%)	7(1.7%)		10(2.4%)	2(0.5%)	
Motor Weakness	16(3.9%)	45(11.0%)		39(9.5%)	22(5.4%)	

DISCUSSION

Vitamin B is a water-soluble vitamin that plays an important role in maintaining the appropriate functioning of the brain and nervous system, along with DNA synthesis.¹⁴ The deficiency of vitamin B is a serious health concern that leads to multiple complications and symptoms, such as dizziness, numbness, anorexia, and major neurological dysfunction and disorders that need appropriate management.¹⁵ The prevalence data of vitamin B deficiency appeared to be rising among older adults and geriatric patients, however, the main cause behind the deficiency remained as nutritional malabsorption and gastrointestinal disorders.¹⁶

The absorption of minerals and nutrients decreases as age increases and causes the lack of intrinsic and intestinal problems. Vitamin B deficiency has a close link with the systemic manifestations and neurological damage which can cause neuropsychiatric symptoms.¹⁷ The neurological symptoms are closely associated with the unavailability of appropriate nutrition or genetic disorders.¹⁸ The results of this study are comparable with the data or similar studies presented worldwide. In our study, the mean age was 46.9±11.5 years. In a study by Andres E, et al,⁸ the mean age was 40.0 years. Another study noted the mean age to be 45.7+ 5.6 years.¹⁹ In the present study, 172 (68.0%) were male while 81

(32.0%) were female.

A study reported that 46% of males and 54% of females.²⁰ There were 48% males and 52% females in the study conducted on a similar pattern.²¹ In the current study, neurological manifestation distribution showed non-traumatic compressive myopathy in 52 (20.5%) patients, nerve numbness was 165 (65.2%), optic atrophy in 10 (3.9%), impaired position sensation in 36 (14.2%), impaired vibration sensation 28 (11.1%), ataxia 46 (18.2%), dementia 12 (4.7%) and motor weakness was noted in 61 (24.1%) patients.²² A study conducted to assess the neurological manifestation and clinical assessment of symptoms reported that (30%) of patients presented with neurological complaints among them ataxia (17%), optic atrophy (4.3%), dementia (4.3%), myelopathy (21%) and numbness documented in (65%) patients.²³

In the study conducted on Neurological manifestations which were observed in terms of memory impairment in 8.7% of the patients and motor weakness in 1.3% of patients with serum B-12 deficiency.²⁴ Neurological manifestations in patients with vitamin B12 deficiency are important and often clinically relevant aspects of this condition.²⁵ Early recognition and diagnosis of vitamin B12 deficiency are essential to prevent the progression of neurological symptoms. Timely intervention, typically through vitamin B12

supplementation, can often reverse these neurological manifestations and improve a patient's overall well-being. However, if left untreated for an extended period, some neurological damage may become permanent.²

Healthcare professionals should remain vigilant, especially when treating individuals at risk of vitamin B12 deficiency, such as vegetarians, vegans, and the elderly, as well as those with certain medical conditions that affect nutrient absorption.⁷ Routine monitoring of vitamin B12 levels and awareness of the potential neurological consequences are critical steps in providing effective care and improving the long-term outcomes for patients with vitamin B12 deficiency.¹⁵ In the present study, stratification of confounders/effect modifiers concerning neurological manifestation, a significant difference was noted in residential status ($p=0.035$) while an insignificant difference was found in age group ($p=0.722$), gender ($p=0.355$), and employment status ($p=0.059$). The study is a cross-sectional design, which restricts the ability to establish causal relationships between vitamin B12 deficiency and neurological manifestations. Additionally, the study was conducted at a single tertiary care hospital, which may limit the generalizability of the findings to other populations or healthcare settings.

CONCLUSION

It is to be concluded that a wide spectrum of neurological symptoms is associated with vitamin B12 deficiency, highlighting its potential impact on neurological health. Nerve numbness stands out as the most prevalent symptom, affecting a significant majority of patients, followed by motor weakness and non-traumatic compressive myelopathy. While optic atrophy and signs of dementia were less frequently observed, they emphasize the critical importance of timely diagnosis and management of this deficiency to prevent severe neurological complications. These

findings underscore the urgency of early detection and treatment of vitamin B12 deficiency to mitigate the risk of a broad range of neurological manifestations.

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Additional Information

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Human Subjects: Consent was obtained by all patients/participants in this study.

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AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Israr Uddin Lashari	1. Conception & Study design and methodology.
2.	Bilal Ahmed Khanzada	2. Analysis of data & interpretation of results.
3.	Awais Bashir	3. Final Approval, editing & quality insurer.
4.	Komal	4. Literature review and referencing.
5.	Noor Nabi Siyal	5. Paper writing.
6.	Mukhtiar Ahmed Abro	6. Data collection & calculations.