Nerve conduction study in vitamin B12 deficiency

1Dr Kallem Venkata Reddy, Associate Professor, Department of General Medicine, Rajiv Gandhi institute of Medical sciences, Adilabad,Telangana,India

2Dr Savita Wawage, Professor, Department of Physiology ,Dr Panjabrao alias Bhausaheb Deshmukh Memorial Medical College Amravati , Maharashtra, India.

3 Dr.U.Sivakumar, Associate Professor , Department of Physiology ,Mahavir institute of medical sciences, Vikarabad ,Telangana, India

Corresponding author: Dr.U.Sivakumar, Associate Professor , Department of Physiology ,Mahavir institute of medical sciences, Vikarabad ,Telangana, India

ABSTRACT

Background: Vitamin B12 deficiency is a common cause of reversible neuropathy. Electrophysiological evaluation using nerve conduction studies (NCS) provides objective evidence of peripheral nerve involvement and helps in early diagnosis.

Material and Methods: This cross-sectional observational study was conducted in a tertiary care hospital between January 2023 and June 2024. A total of 80 participants were enrolled, including 40 patients with confirmed vitamin B12 deficiency (serum B12 <200 pg/mL) and 40 healthy controls (serum B12 >300 pg/mL). Motor and sensory NCS were performed on median, ulnar, tibial, peroneal, and sural nerves using standard techniques. Parameters analyzed included distal latency, amplitude, and conduction velocity. Data were compared between groups using independent t-test and chi-square test, with p <0.05 considered statistically significant.

Results: The mean age of patients was 44.6 ± 11.2 years compared to 43.1 ± 10.8 years in controls (p = 0.56). Paresthesia (65%) and gait disturbance (30%) were the most frequent symptoms in the deficiency group. Serum vitamin B12 levels were significantly lower in patients (142.5 ± 28.3 pg/mL) than in controls (418.6 ± 61.4 pg/mL, p <0.001). Motor studies showed prolonged latencies, reduced CMAP amplitudes, and slowed conduction velocities in vitamin B12–deficient patients. For example, tibial nerve conduction velocity was 42.5 ± 3.8 m/s versus 49.6 ± 3.7 m/s in controls (p <0.001). Sensory studies revealed reduced SNAP amplitudes and slower velocities, with sural nerve conduction velocity at 44.2 ± 3.6 m/s compared to 50.5 ± 4.0 m/s in controls (p <0.001).

Conclusion: Vitamin B12 deficiency is associated with significant sensorimotor conduction abnormalities, predominantly affecting distal nerves. Early detection by NCS may help guide timely therapeutic intervention and prevent irreversible neuropathic changes.

Keywords: Vitamin B12 deficiency; neuropathy; nerve conduction study; sensorimotor neuropathy; electrophysiology

INTRODUCTION

Vitamin B_{12} (cobalamin) is an essential cofactor for methionine synthase and methylmalonyl-CoA mutase; its deficiency impairs myelin maintenance and neuronal metabolism and may lead to a spectrum of neurological manifestations including myelopathy, cognitive dysfunction and peripheral neuropathy. Recent clinical reviews emphasize that biochemical diagnosis of B_{12} deficiency is complex (no single gold-standard test) and that clinical assessment remains critical for interpretation of laboratory results. [1,2]

Peripheral neuropathy is among the common neurologic complications of B_{12} deficiency, but its reported frequency and electrophysiological patterns vary widely between studies. Some cohorts have reported clinical neuropathy in a majority of patients with neurologic B_{12} syndrome, while electrophysiological abnormalities are detected in a variable proportion (roughly one-half in several series), reflecting differences in patient selection, timing of evaluation and the mix of axonal versus demyelinating features. [2,3] Histopathological and electrodiagnostic studies have

more often supported a predominantly axonal sensorimotor neuropathy, although mixed and demyelinating changes have also been described in certain series. [3,4]

Electrophysiological testing — nerve conduction studies (NCS) — provides objective quantification of peripheral nerve involvement and can detect subclinical abnormalities not apparent on clinical examination. Several recent electrophysiological investigations indicate that B_{12} deficiency may produce reductions in sensory and motor amplitudes and slowing of conduction velocities, particularly in distal nerves such as the sural and peroneal nerves; cold provocation and supplementary biomarkers (for example methylmalonic acid) have been used to unmask or better characterize subtle changes. [4,5] In addition, small-fiber dysfunction that may escape routine NCS is increasingly recognized in B_{12}-deficient states and can be investigated with adjunctive techniques. [6]

Given the variable electrophysiological profile of B_{12}-related neuropathy and the potential for early, reversible neural injury with timely treatment, systematic NCS assessment of patients with confirmed B_{12} deficiency can refine clinical diagnosis and quantify the pattern and severity of peripheral nerve involvement. The present study aimed to compare motor and sensory nerve conduction parameters between patients with documented vitamin B_{12} deficiency and healthy controls, and to identify the nerves most commonly affected electrophysiologically.

MATERIAL AND METHODS

Study design and setting: This was a cross-sectional observational study conducted at a tertiary care teaching hospital in India. Written informed consent was obtained from all participants prior to enrolment.

Sample size: A total of 80 subjects were recruited, comprising 40 patients with documented vitamin B12 deficiency and 20 age- and sex-matched healthy controls. The sample size was selected based on feasibility and prior published studies evaluating peripheral nerve conduction in nutritional neuropathies, ensuring adequate power to detect clinically meaningful differences.

Inclusion criteria

- Adults aged 18–65 years.
- Serum vitamin B12 level <200 pg/mL (deficiency group).
- Healthy volunteers with normal serum vitamin B12 levels (>300 pg/mL) and no neurological symptoms (control group).

Exclusion criteria

- History of diabetes mellitus, chronic alcohol use, thyroid dysfunction, or renal/hepatic impairment.
- Known hereditary neuropathies or exposure to neurotoxic drugs.
- Patients with concurrent folate deficiency (<4 ng/mL).
- Prior treatment with vitamin B12 supplementation within the past 6 months.

Clinical assessment: All participants underwent a detailed history and neurological examination. Standardized proformas were used to record demographic details, clinical features, and laboratory investigations, including serum vitamin B12, folate, fasting glucose, thyroid profile, and renal function tests.

Nerve conduction study protocol: Nerve conduction studies (NCS) were performed using a standard EMG/NCV machine in a temperature-controlled laboratory (maintained at 25°C). Skin temperature was kept above 32°C during testing.

- Motor conduction was assessed in the median, ulnar, common peroneal, and tibial nerves. Parameters measured included distal latency, compound muscle action potential (CMAP) amplitude, and conduction velocity.
- Sensory conduction was tested in the median, ulnar, and sural nerves. Sensory nerve action potential (SNAP) amplitude, latency, and conduction velocity were recorded.
- At least two consecutive responses were obtained for each nerve to ensure reproducibility.

Statistical analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as percentages. Comparisons between the vitamin B12 deficiency group and controls were performed using the independent t-test for continuous data and the chi-square test for categorical data. A p value <0.05 was considered statistically significant.

RESULTS

The gender distribution was comparable between groups (male:female ratio 22:18 vs. 21:19, p = 0.82). The average duration of neurological symptoms among patients was 7.2 ± 3.4 months. Paresthesia was the most common presenting feature (65%), followed by gait disturbances (30%). The mean serum vitamin B12 level was 142.5 ± 28.3 pg/mL in patients compared to 418.6 ± 61.4 pg/mL in controls, which was highly significant (p < 0.001) (Table 1).

Patients with vitamin B12 deficiency exhibited significant abnormalities in motor conduction parameters compared to controls. In the median nerve, distal latency was prolonged (4.9 ± 0.6 ms vs. 3.8 ± 0.5 ms, p < 0.001), CMAP amplitude was reduced (6.2 ± 1.3 mV vs. 8.1 ± 1.2 mV, p < 0.001), and conduction velocity was slower (46.8 ± 3.9 m/s vs. 52.4 ± 3.6 m/s, p < 0.001). Similar patterns were observed in the ulnar, tibial, and peroneal nerves, with consistently prolonged latencies, reduced amplitudes, and slowed conduction velocities, all statistically significant (p < 0.001). The tibial and peroneal nerves were the most affected, showing marked slowing of conduction velocity and reduced CMAP amplitudes (Table 2).

Abnormalities were also evident in sensory conduction studies. The median nerve demonstrated reduced SNAP amplitude (14.5 ± 3.6 µV vs. 21.3 ± 4.1 µV, p < 0.001), prolonged latency (3.8 ± 0.5 ms vs. 3.1 ± 0.4 ms, p < 0.001), and decreased conduction velocity (47.6 ± 4.2 m/s vs. 53.8 ±

3.9 m/s, $p < 0.001$). Comparable findings were noted in the ulnar and sural nerves, with all differences reaching statistical significance. The sural nerve showed the greatest reduction in SNAP amplitude and conduction velocity, suggesting prominent involvement of distal sensory fibers (Table 3).

Table 1. Demographic and Clinical Characteristics of Study Participants

Parameter	Vitamin B12 Deficiency Group (n=40)	Control Group (n=40)	p-value
Age (years, mean ± SD)	44.6 ± 11.2	43.1 ± 10.8	0.56
Male : Female ratio	22 : 18	21 : 19	0.82
Duration of symptoms (months, mean ± SD)	7.2 ± 3.4	–	–
Paresthesia (%)	65%	0%	<0.001
Gait disturbance (%)	30%	0%	<0.001
Serum Vitamin B12 (pg/mL, mean ± SD)	142.5 ± 28.3	418.6 ± 61.4	<0.001

Table 2. Motor Nerve Conduction Parameters

Nerve	Parameter	Vitamin B12 Deficiency (n=40)	Controls (n=40)	p-value
Median nerve	Distal latency (ms)	4.9 ± 0.6	3.8 ± 0.5	<0.001
	CMAP amplitude (mV)	6.2 ± 1.3	8.1 ± 1.2	<0.001
	Conduction velocity (m/s)	46.8 ± 3.9	52.4 ± 3.6	<0.001
Ulnar nerve	Distal latency (ms)	3.7 ± 0.4	3.1 ± 0.3	<0.001
	CMAP amplitude (mV)	6.8 ± 1.1	8.6 ± 1.4	<0.001
	Conduction velocity (m/s)	49.3 ± 3.5	54.7 ± 3.8	<0.001
Tibial nerve	Distal latency (ms)	5.5 ± 0.7	4.2 ± 0.5	<0.001
	CMAP amplitude (mV)	7.1 ± 1.6	9.4 ± 1.5	<0.001
	Conduction velocity (m/s)	42.5 ± 3.8	49.6 ± 3.7	<0.001
Peroneal nerve	Distal latency (ms)	5.1 ± 0.6	4.0 ± 0.5	<0.001
	CMAP amplitude (mV)	3.9 ± 1.1	5.7 ± 1.2	<0.001
	Conduction velocity (m/s)	41.8 ± 4.2	47.5 ± 3.9	<0.001

Table 3. Sensory Nerve Conduction Parameters

Nerve	Parameter	Vitamin B12 Deficiency (n=40)	Controls (n=40)	p-value
Median nerve	SNAP amplitude (µV)	14.5 ± 3.6	21.3 ± 4.1	<0.001
	Sensory latency (ms)	3.8 ± 0.5	3.1 ± 0.4	<0.001
	Conduction velocity (m/s)	47.6 ± 4.2	53.8 ± 3.9	<0.001
Ulnar nerve	SNAP amplitude (µV)	13.2 ± 3.2	19.4 ± 3.8	<0.001
	Sensory latency (ms)	3.6 ± 0.5	3.0 ± 0.3	<0.001
	Conduction velocity (m/s)	48.2 ± 4.1	54.1 ± 3.7	<0.001
Sural nerve	SNAP amplitude (µV)	10.8 ± 2.7	16.9 ± 3.2	<0.001
	Sensory latency (ms)	3.9 ± 0.6	3.2 ± 0.4	<0.001
	Conduction velocity (m/s)	44.2 ± 3.6	50.5 ± 4.0	<0.001

DISCUSSION

In this hospital-based cross-sectional study, patients with vitamin B_{12} deficiency demonstrated clear electrophysiological evidence of a predominantly distal, symmetrical sensorimotor neuropathy, with prolonged distal latencies, reduced CMAP/SNAP amplitudes, and slowed conduction velocities in both upper- and lower-limb nerves. The peroneal (motor) and sural (sensory) nerves showed the largest deviations from control values, consistent with preferential distal involvement. These findings are concordant with prior clinical and electrophysiological series describing an axonal pattern of peripheral nerve injury in B_{12} deficiency and emphasize the tendency for distal sensory fibers to be affected early [7].

The pattern observed in our cohort—reduced amplitudes together with slowing of conduction—suggests predominance of axonal loss with secondary slowing, rather than a pure demyelinating process. Several earlier electrodiagnostic and pathological reports have similarly reported axonal sensorimotor polyneuropathy as the most frequent electrophysiological phenotype in B_{12}-related neuropathy, although mixed or primarily demyelinating features have been reported in select cases, particularly when the deficiency has a prolonged or severe course. Our results therefore align with the larger body of evidence that B_{12} deficiency commonly produces axonal degeneration of distal fibers [8].

Biochemical mechanisms linking cobalamin deficiency to peripheral nerve injury are well described and include impaired methylation, accumulation of methylmalonic acid (MMA), and disrupted myelin maintenance; these metabolic derangements can produce both central (subacute combined degeneration) and peripheral nerve pathology. Routine measurement of B_{12} alone may miss functional deficiency in some patients; the literature supports the complementary role of metabolic markers (MMA, homocysteine) to improve diagnostic sensitivity, especially in patients with subclinical or early neuropathy. This biochemical perspective helps explain why electrophysiological abnormalities may be present even when serum B_{12} values are borderline, and supports integrating metabolic testing into evaluation algorithms for neuropathy [9].

Clinical implications of electrophysiological detection are important. NCS provides objective documentation of peripheral nerve involvement and may reveal subclinical abnormalities that prompt earlier treatment. Several systematic reviews and clinical studies indicate that timely cobalamin replacement can improve symptoms and in some cases partially or fully reverse electrophysiological abnormalities, although the degree of recovery depends on duration and severity of nerve injury at the time of treatment. Thus, early detection by NCS in symptomatic or at-risk patients could facilitate earlier therapeutic intervention and better outcomes, while delayed diagnosis may lead to incomplete recovery [10].

Our findings also highlight the limitation of routine NCS in detecting small-fiber dysfunction; increasing evidence indicates that B_{12} deficiency can involve small myelinated/unmyelinated fibers and may produce symptoms despite normal standard NCS. Adjunctive assessments (skin biopsy for intraepidermal nerve fiber density, quantitative sensory testing, sympathetic skin response) or specialized electrophysiological techniques can uncover such involvement and should be considered when clinical suspicion remains high despite normal routine studies [11-13].

Strengths of the present study include a well-matched control group and comprehensive motor and sensory NCS of multiple nerves. Limitations include a single-center cross-sectional design, lack of routine MMA/homocysteine measurements for all participants, and the absence of longitudinal follow-up to document electrophysiological recovery after cobalamin replacement. In addition, routine NCS cannot assess small-fiber neuropathy comprehensively; future studies should combine routine NCS with small-fiber testing and metabolic markers.

CONCLUSION

This study demonstrates that vitamin B12 deficiency is associated with significant abnormalities in peripheral nerve conduction. Early identification of these electrophysiological changes through nerve conduction studies may aid in timely diagnosis and intervention, thereby preventing progression to irreversible neurological impairment. Routine screening for neuropathy in patients with vitamin B12 deficiency should be considered an important component of clinical practice.

REFERENCES

1. Wolffenbuttel BH, Owen PJ, Ward M, Green R. Vitamin B12. BMJ. 2023 Nov 20;383:e071725. doi: 10.1136/bmj-2022-071725.
2. Schleicher E, Didangelos T, Kotzakioulafi E, Cegan A, Peter A, Kantartzis K. Clinical Pathobiochemistry of Vitamin B12 Deficiency: Improving Our Understanding by Exploring Novel Mechanisms with a Focus on Diabetic Neuropathy. Nutrients. 2023 Jun 1;15(11):2597. doi: 10.3390/nu15112597.
3. Kalita J, Chandra S, Bhoi SK, Agarwal R, Misra UK, Shankar SK, et al. Clinical, nerve conduction and nerve biopsy study in vitamin B12 deficiency neurological syndrome with a short-term follow-up. Nutr Neurosci. 2014 Jul;17(4):156-63. doi: 10.1179/1476830513Y.0000000073.
4. Fang X, Yu M, Zheng D, Gao H, Li W, Ma Y. Electrophysiologic Characteristics of Nitrous-Oxide-Associated Peripheral Neuropathy: A Retrospective Study of 76 Patients. J Clin Neurol. 2023 Jan;19(1):44-51. doi: 10.3988/jcn.2023.19.1.44.
5. Tunç M, Ergün U, Say B, Badem ND, Yapar D, İlhan MN. Electrophysiological profile of serum vitamin B12 levels, correlation with serum methylmalonic acid levels, and determination of subclinical peripheral nerve involvement: Electrophysiological profile and vitamin B12. J Surg Med [Internet]. 2022;6(12):951-5. Available from: https://jsurgmed.com/article/view/7568
6. Qiu F, Wu Y, Cao H, Liu B, Du M, Jiang H, et al. Changes of Peripheral Nerve Function and Vitamin B12 Level in People With Parkinson's Disease. Front Neurol. 2020 Oct 29;11:549159. doi: 10.3389/fneur.2020.549159. Erratum in: Front Neurol. 2021 Jan 28;11:643538. doi: 10.3389/fneur.2020.643538.

7. Chu X, Meng L, Zhang W, Luo J, Wang Z, Yuan Y. Peripheral Nervous System Involvement in Late-Onset Cobalamin C Disease? Front Neurol. 2020 Nov 26;11:594905. doi: 10.3389/fneur.2020.594905.
8. Sakly G, Hellara O, Trabelsi A, Dogui M. Neuropathie périphérique réversible liée au déficit en vitamine B12 [Reversible peripheral neuropathy induced by vitamin B12 deficiency]. Neurophysiol Clin. 2005 Nov-Dec;35(5-6):149-53. French. doi: 10.1016/j.neucli.2005.12.001.
9. Warendorf JK, van Doormaal PTC, Vrancken AFJE, Verhoeven-Duif NM, van Eijk RPA, van den Berg LH, et al. Clinical relevance of testing for metabolic vitamin B12 deficiency in patients with polyneuropathy. Nutr Neurosci. 2022 Dec;25(12):2536-2546. doi: 10.1080/1028415X.2021.1985751.
10. Pratama S, Lauren BC, Wisnu W. The efficacy of vitamin B12 supplementation for treating vitamin B12 deficiency and peripheral neuropathy in metformin-treated type 2 diabetes mellitus patients: A systematic review. Diabetes Metab Syndr. 2022 Oct;16(10):102634. doi: 10.1016/j.dsx.2022.102634.
11. Agircan D, Bal N, Gesoglu-Demir T, Gocmen A, Ethemoglu O. The electrophysiological evaluation of small fiber neuropathy in symptomatic patients with vitamin B12 deficiency before and after treatment. Neurol Sci Neurophysiol. 2024 Jul-Sep;41(3):182-9. doi: 10.4103/nsn.nsn_92_24.
12. Chiaramonte R, Romano M, Vecchio M. A Systematic Review of the Diagnostic Methods of Small Fiber Neuropathies in Rehabilitation. Diagnostics (Basel). 2020 Aug 20;10(9):613. doi: 10.3390/diagnostics10090613.
13. Sun B, Liu LZ, Li YF, Chen ZH, Ling L, Yang F, et al. Clinical Characteristics, Electrophysiology, and Skin Biopsy of 38 Peripheral Neuropathy Cases with Small Fiber Involvement of Various Etiologies. Chin Med J (Engl). 2017 Jul 20;130(14):1683-1688. doi: 10.4103/0366-6999.209897.