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Original Article

Vitamin D Status and Neuropathic Pain Phenotypes in Diabetic Peripheral Neuropathy

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ABSTRACT

Background: Diabetic peripheral neuropathy is a common complication of type 2 diabetes mellitus and presents with heterogeneous painful and sensory phenotypes. Vitamin D deficiency is frequent in diabetic populations, but its relationship with specific neuropathic pain patterns remains insufficiently characterized. Objective: To evaluate the association between serum 25-hydroxyvitamin D status and neuropathic pain phenotypes, pain severity, and sensory findings among adults with type 2 diabetes mellitus and diabetic peripheral neuropathy. Methods: This hospital-based analytical cross-sectional study included 180 adults with type 2 diabetes mellitus and clinical diabetic peripheral neuropathy. Participants were classified as vitamin D deficient, insufficient, or sufficient according to serum 25-hydroxyvitamin D levels. Neuropathic pain was assessed using DN4, visual analogue scale, Neuropathic Pain Symptom Inventory, clinical sensory examination, and modified Toronto Clinical Neuropathy Score. Results: Vitamin D deficiency was present in 104 participants, insufficiency in 49, and sufficiency in 27. DN4-defined painful neuropathy was more frequent in deficient participants than sufficient participants. The deficient group had higher VAS score, NPSI score, modified TCNS score, abnormal monofilament findings, and reduced vibration sense. Vitamin D deficiency remained associated with painful diabetic neuropathy after adjustment for age, sex, diabetes duration, and HbA1c. Conclusion: Vitamin D deficiency was associated with greater painful neuropathy burden and more frequent sensory abnormalities in diabetic peripheral neuropathy. Vitamin D assessment may be a useful supportive component of phenotype-based neuropathy evaluation. Keywords: Vitamin D deficiency; diabetic peripheral neuropathy; neuropathic pain; burning feet; type 2 diabetes; Pakistan.

INTRODUCTION

Diabetes mellitus has become one of the most important non-communicable disease burdens in Pakistan, with national surveys showing a high and increasing prevalence of type 2 diabetes mellitus and prediabetes among adults. This burden is particularly relevant in Punjab, the most populous province of Pakistan, where earlier national data reported substantial glucose intolerance and where urbanization, sedentary behavior, obesity, delayed diagnosis, and variable access to preventive care continue to increase diabetes-related complications. The epidemiological estimates from Pakistan also vary across surveys because of differences in sampling methods, diagnostic criteria, and population characteristics, which supports the need for locally generated clinical evidence from hospital settings where patients commonly present with established complications (1–4).

Diabetic peripheral neuropathy is one of the most frequent and disabling complications of type 2 diabetes mellitus and is strongly associated with longer diabetes duration and poor glycemic control. It typically begins distally in the feet and may progress proximally, producing pain, sensory loss, impaired balance, sleep disturbance, reduced mobility, foot ulcer risk, and substantial impairment in quality of life. Although diabetic peripheral neuropathy is often discussed as a single complication, its clinical expression is heterogeneous. Some patients present predominantly with burning feet and nocturnal pain, whereas others experience tingling, pins-and-needles sensations, electric shock-like attacks, evoked pain from light touch, or numbness with loss of protective sensation. This heterogeneity is clinically important because painful and painless neuropathy may reflect different sensory profiles, degrees of small- and large-fiber involvement, and different patterns of symptom burden despite sharing the same underlying diagnosis (5–9).

The recognition of neuropathic pain phenotypes has improved the clinical interpretation of diabetic peripheral neuropathy beyond simple pain-intensity scoring. The Pain in Neuropathy Study showed that painful and painless diabetic neuropathy are associated with distinct somatosensory phenotypes, supporting the need to characterize patients according to symptom quality as well as overall severity (10). Phenotype-based assessment is also relevant for treatment selection and clinical trial interpretation because burning pain, paroxysmal pain, evoked pain, paresthesia-dominant symptoms, and numbness-dominant presentations may not respond uniformly to the same therapeutic strategies (11). Structured instruments such as the Neuropathic Pain Symptom Inventory and DN4 questionnaire allow neuropathic symptoms to be categorized more consistently by capturing burning, pressing, paroxysmal, evoked, and paresthesia-related features, thereby improving the reproducibility of clinical pain assessment in diabetic neuropathy research (12,13).

Vitamin D has traditionally been examined in relation to calcium metabolism and bone health, but increasing evidence suggests that it may also influence neuromuscular function, inflammatory regulation, and pain signaling. Vitamin D receptors and vitamin D–related pathways have been identified in tissues involved in nociception and neuronal regulation, and experimental evidence suggests potential interactions with inflammatory mediators, neurotrophic factors, immune signaling, and sensory neuronal excitability (14). Clinically, low vitamin D levels have been reported in several chronic pain states, although the magnitude and consistency of association differ across populations, disease mechanisms, and supplementation protocols (15). In patients with type 2 diabetes, vitamin D deficiency may coexist with several neuropathy-related risk factors, including obesity, limited sunlight exposure, reduced physical activity, chronic inflammation, poor glycemic control, and longer disease duration, making its relationship with neuropathic pain clinically plausible but methodologically complex.

Evidence linking vitamin D status with diabetic peripheral neuropathy has increased in recent years, but important uncertainties remain. Reviews have suggested that vitamin D may have a role in the prevention or treatment of diabetic neuropathy, although the quality of evidence remains limited by heterogeneity in populations, definitions of deficiency, supplementation regimens, and outcome measures (16). Observational evidence has shown that the association between diabetic peripheral neuropathy and vitamin D may depend on vitamin D status, while other studies have reported that vitamin D deficiency is associated with painful diabetic neuropathy and small-fiber-related features (17,18). Additional clinical work has linked vitamin D status with neuropathic pain and balance impairment in diabetic patients, and systematic reviews have suggested possible pain reduction after vitamin D supplementation, although trial samples are generally small and follow-up durations are short (19–21). Pakistani studies have also reported improvement in painful diabetic neuropathy after high-dose or single-dose vitamin D therapy, supporting the local relevance of investigating vitamin D in this population (22,23). However, much of the existing literature evaluates neuropathy presence or total pain intensity rather than differentiating pain phenotypes, and meta-analytic evidence continues to emphasize the need for better-defined clinical subgroup analyses (24).

This knowledge gap is important because patients with diabetic peripheral neuropathy do not present with a uniform pain experience. A patient with severe burning feet may differ biologically and clinically from a patient with electric shock-like paroxysms, evoked allodynia, tingling-dominant discomfort, or painless numbness with sensory loss. If low vitamin D status is associated more strongly with selected painful phenotypes rather than with neuropathy as a broad diagnosis, vitamin D testing may have additional value as a supportive clinical assessment in selected patients with painful diabetic neuropathy, particularly in resource-limited settings where deficiency is common and advanced neurophysiological testing is not always available. Such an association would not prove causality, because diabetic neuropathy is influenced by glycemic exposure, diabetes duration, obesity, renal function, vitamin B12 status, thyroid disease, medications, vascular risk factors, and lifestyle factors. Nevertheless, identifying phenotype-specific clinical patterns may improve patient-centered assessment and guide future interventional studies.

The present hospital-based analytical study was therefore designed to evaluate the association between serum 25-hydroxyvitamin D status and neuropathic pain phenotypes among adults with type 2 diabetes mellitus and clinical diabetic peripheral neuropathy in Punjab, Pakistan. Using a PICO framework, the population comprised adults with type 2 diabetes and diabetic peripheral neuropathy, the exposure was vitamin D deficiency or insufficiency, the comparison group was patients with sufficient vitamin D status, and the outcomes were dominant neuropathic pain phenotype, pain severity, DN4 score, Neuropathic Pain Symptom Inventory score, sensory examination findings, and modified Toronto Clinical Neuropathy Score. The primary objective was to determine whether vitamin D deficiency was associated with specific neuropathic pain phenotypes, particularly burning, paroxysmal, evoked, paresthesia-dominant, numbness-dominant, or mixed presentations. The secondary objective was to examine whether vitamin D deficiency was independently associated with painful diabetic neuropathy after adjustment for relevant clinical confounders.

MATERIAL AND METHODS

This hospital-based analytical cross-sectional study was conducted in the Medicine and Diabetes outpatient departments of a tertiary care hospital in Punjab, Pakistan, over a six-month data collection period. The study was designed to evaluate whether serum 25-hydroxyvitamin D status was associated with the clinical phenotype and severity of neuropathic pain among adults with type 2 diabetes mellitus and diabetic peripheral neuropathy. A cross-sectional analytical design was used because vitamin D status, neuropathic pain characteristics, sensory findings, and clinical neuropathy severity were assessed during the same clinical evaluation rather than through longitudinal follow-up.

The study population consisted of adult male and female patients with type 2 diabetes mellitus who presented for routine diabetes follow-up or neuropathy-related complaints and had symptoms or signs consistent with diabetic peripheral neuropathy. Participants were selected using non-probability consecutive sampling, whereby every eligible patient attending the outpatient departments during the study period was invited to participate until the required sample size was achieved. Patients were eligible if they were 30 to 75 years of age, had a documented diagnosis of type 2 diabetes mellitus for at least one year, and reported symptoms or demonstrated signs suggestive of peripheral neuropathy, including burning pain, numbness, tingling, pins-and-needles sensation, electric shock-like pain, stabbing pain, nocturnal worsening of symptoms, reduced distal sensation, or impaired protective sensation in the feet. Patients were excluded if they had an alternative or contributory cause of peripheral neuropathy, including chronic alcohol use, chronic kidney disease stage 4 or 5, hypothyroidism, vitamin B12 deficiency, active malignancy, history of chemotherapy, stroke with residual sensory deficit, spinal disease with radiculopathy, recent foot trauma, pregnancy, or high-dose vitamin D supplementation during the preceding three months.

Eligible patients were approached during outpatient visits, and the study purpose, procedures, potential risks, and voluntary nature of participation were explained before enrollment. Written informed consent was obtained before data collection. Each participant was interviewed and examined in a separate clinical area to maintain privacy and to reduce information bias. Data were collected using a structured proforma administered in a standardized sequence. The first section recorded sociodemographic and lifestyle variables, including age, sex, residence, occupation, smoking status, sunlight exposure, supplement use, and relevant medical history. The second section recorded diabetes-related clinical characteristics, including duration of diabetes, treatment modality, body mass index, blood pressure, fasting blood glucose, HbA1c, history of hypertension, history of dyslipidemia, and other relevant comorbidities. Duration of diabetes was calculated in completed years from the time of first diagnosis of type 2 diabetes mellitus.

The exposure variable was serum 25-hydroxyvitamin D status. A venous blood sample was obtained from each participant for serum 25-hydroxyvitamin D measurement using the hospital laboratory's standard assay procedure. Vitamin D status was operationally categorized into three groups: deficient, defined as serum 25-hydroxyvitamin D concentration below 20 ng/mL; insufficient, defined as 20 to 29 ng/mL; and sufficient, defined as 30 ng/mL or above. Additional laboratory investigations included HbA1c, fasting blood glucose, serum creatinine, thyroid profile, and vitamin B12 assessment when clinically indicated to support characterization of diabetes control, identify relevant confounding factors, and exclude alternative causes of neuropathy.

Neuropathic pain was assessed using both symptom history and standardized clinical instruments. Pain intensity was recorded using a 10-cm visual analogue scale, where 0 represented no pain and 10 represented the worst pain experienced by the patient. The DN4 questionnaire was used to support classification of neuropathic pain, with a score of 4 or higher considered suggestive of painful neuropathy (13). Symptom pattern was assessed using the Neuropathic Pain Symptom Inventory, which captures clinically relevant dimensions of neuropathic pain, including burning pain, pressing pain, paroxysmal pain, evoked pain, paresthesia, and dysesthesia (12). The primary outcome was dominant neuropathic pain phenotype. Dominant phenotype was assigned according to the symptom reported by the patient as the most frequent, severe, or clinically troublesome complaint during the preceding symptomatic period. Burning phenotype was defined by predominant burning or hot pain in the feet; paroxysmal phenotype by predominant electric shock-like, stabbing, or shooting attacks; evoked pain phenotype by pain triggered by light touch, socks, bedsheet contact, mild pressure, or similar non-painful stimuli; paresthesia-dominant phenotype by predominant tingling, pins-and-needles, or crawling sensations; numbness-dominant phenotype by predominant loss of sensation, dead feeling, or reduced awareness of the feet; and mixed phenotype by the absence of a single dominant symptom or the presence of two or more similarly prominent neuropathic symptom clusters.

A standardized neurological examination of both feet was performed for all participants. Light touch, pinprick sensation, temperature sensation, vibration perception, ankle reflexes, and protective sensation were assessed using routine clinical procedures. Vibration perception was tested with a 128-Hz tuning fork over the great toe, and protective sensation was assessed using a 10-g monofilament at standard plantar foot sites. An abnormal monofilament test was defined as inability to perceive pressure at one or more tested protective-sensation sites according to the clinical examination protocol. Neuropathy severity was graded using the modified Toronto Clinical Neuropathy Score, which combines neuropathic symptoms, reflex assessment, and sensory examination findings, with higher scores indicating greater neuropathy severity (25). To reduce measurement variability, the same structured clinical approach was followed for all participants, and symptom instruments were administered in the same order.

The main outcome was the association between vitamin D category and dominant neuropathic pain phenotype. Secondary outcomes included DN4 score, frequency of DN4-defined painful neuropathy, visual analogue scale pain score, Neuropathic Pain Symptom Inventory total score, abnormal

monofilament testing, reduced vibration sense, and modified Toronto Clinical Neuropathy Score. Potential confounders considered in the analysis included age, sex, duration of diabetes, HbA1c, body mass index, hypertension, dyslipidemia, and other clinically relevant variables available in the dataset. Painful diabetic neuropathy was operationally defined as diabetic peripheral neuropathy with DN4 score of 4 or higher.

The sample size was calculated using the expected frequency of vitamin D deficiency among patients with type 2 diabetes mellitus and diabetic peripheral neuropathy, with a 95% confidence level and 5% margin of error. After allowing for incomplete data, the final sample size was set at 180 participants. This sample was then categorized into deficient, insufficient, and sufficient vitamin D groups for comparative analysis. Data were reviewed for completeness and internal consistency before statistical analysis. Missing or implausible values were checked against the source proforma where possible, and variables with incomplete entries were analyzed using available-case analysis without imputation.

Data were entered and analyzed using SPSS version 26. Continuous variables were summarized as mean and standard deviation when approximately normally distributed and as median with interquartile range when distributional assumptions were not met. Categorical variables were summarized as frequencies and percentages using the relevant group denominator. Baseline clinical characteristics, neuropathic pain scores, sensory examination findings, and pain phenotype distributions were compared across vitamin D categories. Chi-square test or Fisher's exact test was used for categorical variables according to expected cell counts. One-way analysis of variance was used for normally distributed continuous variables across three vitamin D groups, while the Kruskal-Wallis test was used for non-normally distributed continuous variables. Logistic regression analysis was performed to determine whether vitamin D deficiency was independently associated with painful diabetic neuropathy after adjustment for age, sex, duration of diabetes, and HbA1c. Adjusted odds ratios with 95% confidence intervals were reported, and vitamin D sufficiency was treated as the reference category. A p-value less than 0.05 was considered statistically significant.

Ethical conduct was maintained throughout the study by enrolling only consenting participants, preserving confidentiality of patient information, and using anonymized data for analysis. Data collection was limited to clinically relevant interview responses, physical examination findings, and laboratory parameters required for the study objectives. All records were checked for accuracy before analysis, and the same operational definitions were applied throughout the dataset to support reproducibility and reduce classification bias.

RESULTS

A total of 180 adults with type 2 diabetes mellitus and clinical diabetic peripheral neuropathy were included in the analysis. The mean age of the participants was 52.6 ± 9.2 years, and the study population included 98 females and 82 males. The mean duration of diabetes was 8.1 ± 4.6 years, and overall glycemic control was suboptimal, with a mean HbA1c of 8.3 ± 1.4%. According to serum 25-hydroxyvitamin D concentration, 104 participants were classified as vitamin D deficient, 49 as vitamin D insufficient, and 27 as vitamin D sufficient.

Table 1. Baseline Characteristics of Participants According to Vitamin D Status

Variable	Deficient <20 ng/mL n=104	Insufficient 20–29 ng/mL n=49	Sufficient ≥30 ng/mL n=27	p-value
Age, years	53.6 ± 9.2	52.1 ± 8.7	50.4 ± 9.8	0.28
Female sex	60 (57.7)	25 (51.0)	13 (48.1)	0.59
Duration of diabetes, years	9.2 ± 4.8	7.4 ± 4.1	5.9 ± 3.6	0.003
HbA1c, %	8.7 ± 1.4	8.1 ± 1.3	7.6 ± 1.1	0.001
BMI, kg/m²	28.2 ± 4.7	27.0 ± 4.2	26.4 ± 3.9	0.14
Hypertension	58 (55.8)	23 (46.9)	11 (40.7)	0.25

Values are presented as mean ± SD or n (%). BMI, body mass index; HbA1c, glycated hemoglobin.

Participants with vitamin D deficiency had longer diabetes duration and poorer glycemic control than those with sufficient vitamin D status. Mean diabetes duration was 9.2 ± 4.8 years in the deficient group compared with 5.9 ± 3.6 years in the sufficient group, while mean HbA1c was 8.7 ± 1.4% and 7.6 ± 1.1%, respectively. Age, sex distribution, BMI, and hypertension frequency did not differ substantially across vitamin D categories.

Table 2. Neuropathic Pain Severity and Sensory Findings According to Vitamin D Status

Outcome	Deficient <20 ng/mL n=104	Insufficient 20–29 ng/mL n=49	Sufficient ≥30 ng/mL n=27	p-value
DN4 score ≥4	89 (85.6)	36 (73.5)	15 (55.6)	0.002
Pain VAS score	6.7 ± 1.8	5.6 ± 1.9	4.4 ± 2.0	<0.001
NPSI total score	48.5 ± 14.8	40.2 ± 13.5	31.6 ± 12.9	<0.001
Modified TCNS score	12.9 ± 4.1	10.8 ± 3.8	8.7 ± 3.4	<0.001
Abnormal monofilament test	61 (58.7)	22 (44.9)	9 (33.3)	0.035
Reduced vibration sense	68 (65.4)	25 (51.0)	10 (37.0)	0.021

Values are presented as mean ± SD or n (%). DN4, Douleur Neuropathique 4 questionnaire; NPSI, Neuropathic Pain Symptom Inventory; TCNS, Toronto Clinical Neuropathy Score; VAS, visual analogue scale.

Neuropathic pain and sensory impairment showed a graded pattern across vitamin D categories. DN4-defined painful neuropathy was present in 89 of 104 participants with vitamin D deficiency, 36 of 49 with insufficiency, and 15 of 27 with sufficient vitamin D status. Pain intensity followed the same direction, with mean VAS scores of 6.7 ± 1.8, 5.6 ± 1.9, and 4.4 ± 2.0 across deficient, insufficient, and sufficient groups, respectively. NPSI total score and modified TCNS score were also highest in the deficient group. Objective sensory findings were more frequent among deficient participants, including abnormal monofilament testing in 61 participants and reduced vibration sense in 68 participants.

Table 3. Pairwise Effect Estimates for Pain and Neuropathy Severity Compared With Vitamin D Sufficiency

Outcome	Comparison	Mean Difference	95% CI
Pain VAS score	Deficient vs sufficient	2.30	1.44 to 3.16
Pain VAS score	Insufficient vs sufficient	1.20	0.25 to 2.15
NPSI total score	Deficient vs sufficient	16.90	11.11 to 22.69
NPSI total score	Insufficient vs sufficient	8.60	2.30 to 14.90
Modified TCNS score	Deficient vs sufficient	4.20	2.66 to 5.74
Modified TCNS score	Insufficient vs sufficient	2.10	0.40 to 3.80
Duration of diabetes, years	Deficient vs sufficient	3.30	1.62 to 4.98
Duration of diabetes, years	Insufficient vs sufficient	1.50	-0.31 to 3.31
HbA1c, %	Deficient vs sufficient	1.10	0.59 to 1.61
HbA1c, %	Insufficient vs sufficient	0.50	-0.06 to 1.06

Mean differences were derived from reported group means, standard deviations, and sample sizes. CI, confidence interval; HbA1c, glycated hemoglobin; NPSI, Neuropathic Pain Symptom Inventory; TCNS, Toronto Clinical Neuropathy Score; VAS, visual analogue scale.

Compared with participants with sufficient vitamin D levels, those with vitamin D deficiency had a 2.30-point higher mean VAS pain score, a 16.90-point higher mean NPSI total score, and a 4.20-point higher modified TCNS score. Participants with vitamin D insufficiency also had higher pain and neuropathy scores than the sufficient group, but the magnitude of difference was smaller than that observed in the deficient group. The deficient group also had longer diabetes duration and higher HbA1c values than the sufficient group.

In crude comparative analysis, vitamin D deficiency was associated with higher odds of DN4-defined painful neuropathy, abnormal monofilament testing, and reduced vibration sense compared with vitamin D sufficiency. The odds of DN4 score ≥4 were 4.75 times higher in deficient participants than in sufficient participants. Vitamin D insufficiency showed the same direction of association, but the confidence intervals for DN4-defined painful neuropathy, abnormal monofilament testing, and reduced vibration sense included the null value.`

Table 4. Crude Associations of Vitamin D Status With Painful Neuropathy and Sensory Abnormalities

Outcome	Comparison	Odds Ratio	95% CI
DN4 score ≥4	Deficient vs sufficient	4.75	1.86 to 12.10
DN4 score ≥4	Insufficient vs sufficient	2.22	0.82 to 5.96
Abnormal monofilament test	Deficient vs sufficient	2.84	1.16 to 6.91
Abnormal monofilament test	Insufficient vs sufficient	1.63	0.61 to 4.33
Reduced vibration sense	Deficient vs sufficient	3.21	1.33 to 7.74
Reduced vibration sense	Insufficient vs sufficient	1.77	0.68 to 4.63

Odds ratios were derived from reported group counts. Vitamin D sufficiency was used as the reference category. CI, confidence interval; DN4, Douleur Neuropathique 4 questionnaire.

Table 5. Adjusted Association Between Vitamin D Deficiency and Painful Diabetic Neuropathy

Predictor	Reference Category	Adjusted Odds Ratio	95% CI	p-value
Vitamin D deficiency	Vitamin D sufficiency	3.26	1.32 to 8.06	<0.05

Model adjusted for age, sex, duration of diabetes, and HbA1c. Painful diabetic neuropathy was defined as DN4 score ≥4. CI, confidence interval; HbA1c, glycated hemoglobin.

After adjustment for age, sex, diabetes duration, and HbA1c, vitamin D deficiency remained independently associated with painful diabetic neuropathy. Participants with vitamin D deficiency had 3.26 times higher adjusted odds of DN4-defined painful neuropathy compared with participants with sufficient vitamin D levels.

Burning pain was described as the most frequent dominant neuropathic pain phenotype in the study population and was reported more often among participants with vitamin D deficiency. Paroxysmal pain, including electric shock-like and stabbing pain, and evoked pain triggered by touch, socks, bedsheet contact, or mild pressure were also described more frequently among participants with low vitamin D status. Numbness-dominant symptoms were described as relatively more common among participants with sufficient vitamin D levels. However, phenotype-specific frequencies, percentages, p-values, and effect estimates were not available in the supplied results; therefore, formal tabulation of neuropathic pain phenotype distribution by vitamin D category could not be validly performed from the available aggregate data.

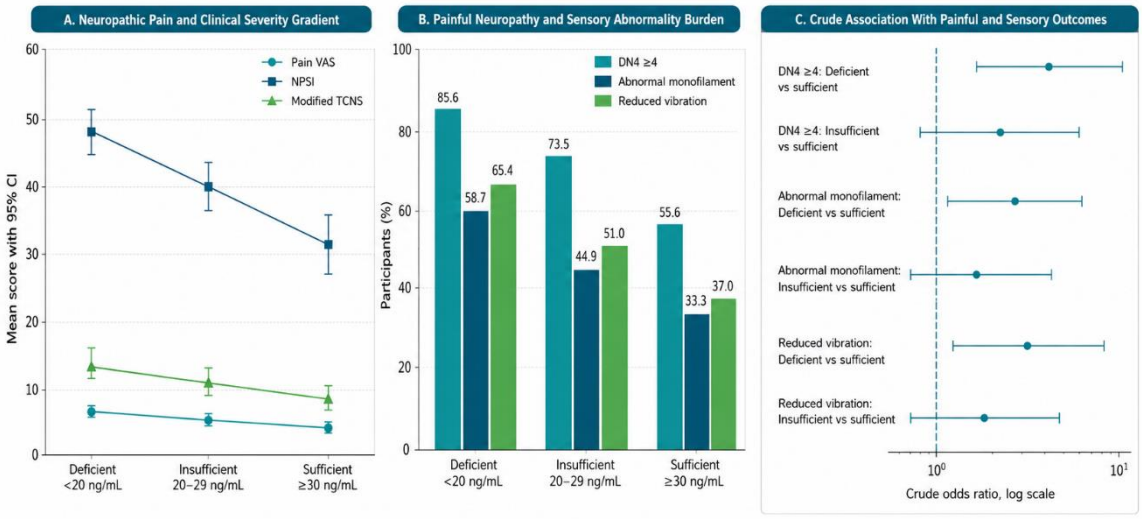

Figure 1 Vitamin D Status and Neuropathic Burden in Diabetic Peripheral Neuropathy

The panelled figure demonstrates a graded increase in neuropathic burden with declining vitamin D status. Participants with vitamin D deficiency had the highest mean pain VAS score, NPSI total score, and modified TCNS score, with mean values of 6.7, 48.5, and 12.9, respectively, compared with 4.4, 31.6, and 8.7 among participants with sufficient vitamin D levels. The proportion of DN4-defined painful neuropathy was also highest in the deficient group at 85.6%, followed by 73.5% in the insufficient group

and 55.6% in the sufficient group. Objective sensory abnormalities followed the same direction, with abnormal monofilament testing in 58.7% and reduced vibration sense in 65.4% of vitamin D-deficient participants compared with 33.3% and 37.0% among vitamin D-sufficient participants. Crude association estimates further supported this gradient, showing higher odds of DN4-defined painful neuropathy in vitamin D-deficient participants compared with the sufficient group, with an odds ratio of 4.75 and 95% confidence interval of 1.86 to 12.10. These patterns suggest that vitamin D deficiency is associated with both greater painful symptom burden and more frequent objective sensory impairment in diabetic peripheral neuropathy.

DISCUSSION

The present hospital-based analytical study found that vitamin D deficiency was highly prevalent among adults with type 2 diabetes mellitus and clinical diabetic peripheral neuropathy, with 104 of 180 participants classified as deficient. The findings also showed a consistent clinical gradient across vitamin D categories, where patients with deficient vitamin D status had longer diabetes duration, poorer glycemic control, higher DN4 scores, greater pain intensity, higher Neuropathic Pain Symptom Inventory scores, more severe modified Toronto Clinical Neuropathy Scores, and more frequent objective sensory abnormalities than patients with sufficient vitamin D levels. This pattern is clinically important because diabetic peripheral neuropathy is not limited to sensory loss; it is a complex complication associated with pain, impaired protective sensation, disability, balance impairment, foot ulceration risk, and reduced quality of life. The observed association between vitamin D deficiency and painful neuropathy therefore adds to the growing evidence that metabolic and nutritional factors may contribute to the heterogeneity of neuropathic symptom expression in patients with diabetes (5–9).

The high frequency of vitamin D deficiency in this study is consistent with the wider clinical context of diabetes care in Pakistan, where the burden of type 2 diabetes and prediabetes is substantial and continues to increase. National and regional surveys have shown that diabetes is common in Pakistani adults, including populations from Punjab, and that estimates vary across studies because of differences in sampling and diagnostic methods (1–4). In such settings, patients often present late with established complications, including diabetic peripheral neuropathy. The deficient group in the present study also had longer diabetes duration and higher HbA1c values than the sufficient group, both of which are recognized risk factors for neuropathy. This indicates that vitamin D deficiency may coexist with other neuropathy-promoting exposures rather than acting as an isolated factor. Nevertheless, the association between vitamin D deficiency and DN4-defined painful neuropathy persisted after adjustment for age, sex, diabetes duration, and HbA1c, suggesting that low vitamin D status may provide additional clinical information beyond conventional diabetes-related risk indicators.

Painful neuropathy was more frequent among participants with lower vitamin D levels. DN4-defined painful neuropathy was present in 85.6% of vitamin D-deficient participants compared with 55.6% of participants with sufficient vitamin D status. Pain severity followed the same direction, with mean VAS scores of 6.7 in the deficient group, 5.6 in the insufficient group, and 4.4 in the sufficient group. The NPSI total score also showed a graded pattern across vitamin D categories, indicating that the association was not limited to a binary definition of painful neuropathy but extended to overall neuropathic symptom burden. These findings are consistent with previous observational evidence reporting an association between low vitamin D status and painful diabetic neuropathy, including studies that suggested a stronger relationship in patients with painful or small-fiber-related neuropathic features (17,18). They also align with clinical studies and reviews suggesting that vitamin D supplementation may reduce pain in painful diabetic neuropathy, although the available interventional evidence remains limited by small sample sizes, heterogeneous dosing schedules, and short follow-up periods (20–23).

The dominant clinical pattern described in this study was burning pain, followed by paroxysmal and evoked pain among patients with low vitamin D status. Although exact phenotype-specific frequencies

were not available in the supplied results, the reported direction of findings is biologically plausible. Burning pain is often considered a clinical marker of small-fiber involvement, whereas paroxysmal electric shock-like pain may reflect abnormal sensory nerve excitability. Evoked pain from socks, bedsheet contact, or light pressure may indicate altered peripheral and central pain processing. Previous work has emphasized that painful and painless diabetic neuropathy can have distinct somatosensory profiles, and that phenotype-based assessment may be more informative than classifying neuropathy solely by presence, absence, or total pain score (10,11). The use of DN4 and NPSI in the present study therefore strengthens clinical characterization by capturing symptom quality as well as pain intensity (12,13). However, because phenotype-specific counts were not reported, the phenotype findings should be interpreted as descriptive and hypothesis-generating rather than definitive comparative evidence.

Objective sensory findings also differed across vitamin D categories. Abnormal monofilament testing and reduced vibration sense were more frequent in vitamin D-deficient participants than in participants with sufficient vitamin D status. These findings suggest that low vitamin D status was associated not only with subjective pain symptoms but also with clinically detectable sensory impairment. The modified Toronto Clinical Neuropathy Score was also higher in the deficient group, indicating greater overall neuropathy severity (25). This is relevant because loss of protective sensation and impaired vibration perception are clinically important markers of foot injury risk and advanced neuropathy. Diabetic neuropathy develops through complex metabolic, vascular, inflammatory, and neurodegenerative mechanisms, and vitamin D may be one component within this broader pathophysiological network rather than a single causal determinant (7–9).

Several biological mechanisms may explain the observed association between vitamin D deficiency and painful neuropathic features. Vitamin D has potential interactions with inflammatory pathways, immune regulation, neurotrophic factors, and sensory neuronal signaling, all of which may influence pain sensitivity and nerve function (14). Low vitamin D levels have also been associated with chronic pain states, although the clinical strength of this association varies across conditions (15). In diabetes, vitamin D deficiency may cluster with obesity, reduced sunlight exposure, limited physical activity, poor diet, chronic inflammation, and inadequate glycemic control. These overlapping pathways make it plausible that vitamin D deficiency may contribute to neuropathic pain vulnerability or serve as a marker of a broader adverse metabolic state. The cross-sectional nature of this study, however, prevents determination of directionality; it cannot establish whether vitamin D deficiency preceded neuropathic pain, resulted from reduced mobility and sunlight exposure, or simply coexisted with more severe diabetes-related complications.

The clinical implication of these findings is that vitamin D assessment may be useful as a supportive component of evaluation in selected patients with painful diabetic peripheral neuropathy, particularly those with severe burning pain, nocturnal symptoms, high DN4 scores, and objective sensory impairment. This does not mean that vitamin D testing should replace established neuropathy assessment, glycemic optimization, foot-care education, risk-factor control, or evidence-based neuropathic pain management. Rather, vitamin D status may help identify a potentially modifiable deficiency in patients with painful neuropathy, especially in resource-limited settings where deficiency is common and advanced neurophysiological testing is not routinely accessible. Any recommendation for supplementation should remain individualized and should follow clinical guidelines, baseline deficiency status, safety considerations, and follow-up monitoring.

This study has several limitations. First, the hospital-based design may limit generalizability because patients attending tertiary outpatient departments may have more severe diabetes, more neuropathic symptoms, or more comorbidities than community-based diabetic populations. Second, the cross-sectional analytical design allows assessment of association but not causality or temporal sequence. Third, vitamin D was measured at a single time point, so seasonal variation, long-term vitamin D exposure, and changes in supplementation or sunlight exposure could not be fully evaluated. Fourth,

although the analysis adjusted for age, sex, diabetes duration, and HbA1c, residual confounding may remain from body mass index, physical activity, diet, sunlight exposure, renal function, vitamin B12 status, medication use, neuropathic pain treatment, and comorbid vascular disease. Fifth, phenotype-specific frequencies were not available in the reported aggregate results, which limited formal statistical comparison of burning, paroxysmal, evoked, paresthesia-dominant, numbness-dominant, and mixed presentations across vitamin D categories.

Despite these limitations, the study contributes useful local evidence by linking vitamin D status with neuropathic pain severity, structured neuropathic symptom scores, clinical neuropathy grading, and objective sensory findings among patients with type 2 diabetes and diabetic peripheral neuropathy. Its main strength is the use of clinically interpretable tools, including DN4, NPSI, sensory examination, monofilament testing, vibration assessment, and modified TCNS, rather than relying only on a single pain-intensity score. Future research should include multicenter recruitment, community-based sampling, standardized laboratory assessment of vitamin D and competing neuropathy causes, complete phenotype-specific reporting, and prospective follow-up to determine whether baseline vitamin D status predicts progression or persistence of painful neuropathy. Randomized controlled trials with adequate sample size and phenotype-stratified outcomes are also needed to determine whether correction of vitamin D deficiency improves specific neuropathic pain phenotypes.

CONCLUSION

Vitamin D deficiency was common among adults with type 2 diabetes mellitus and clinical diabetic peripheral neuropathy and was associated with greater neuropathic pain burden, higher DN4-defined painful neuropathy frequency, higher VAS and NPSI scores, more severe modified TCNS scores, and more frequent sensory abnormalities. Burning, paroxysmal, and evoked pain patterns were described more often among patients with low vitamin D status, whereas numbness-dominant symptoms were relatively more common among patients with sufficient vitamin D levels, although exact phenotype-specific frequencies should be reported in future analyses to support formal comparison. After adjustment for age, sex, diabetes duration, and HbA1c, vitamin D deficiency remained associated with painful diabetic neuropathy, indicating that vitamin D status may serve as a clinically relevant supportive marker in selected patients with painful diabetic peripheral neuropathy. These findings support the value of phenotype-based neuropathy assessment and suggest that vitamin D evaluation may be considered as part of comprehensive diabetic neuropathy care, while prospective and interventional studies are required to clarify causality and therapeutic relevance.

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