Research Article

Comparison Of Vitamin D Level In Type 2 Diabetes Mellitus Between Those With Peripheral Neuropathy And Without: A Comparative Cross-Sectional Study

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Abstract

Diabetic peripheral neuropathy (DPN) is one of the most common chronic complications of type 2 diabetes mellitus (T2DM). Vitamin D deficiency has been implicated in the development of DPN through its neuroprotective and anti-inflammatory properties; however, evidence from the Indonesian population remains limited. This study aimed to compare serum vitamin D levels between T2DM patients with and without DPN. A comparative cross-sectional study was conducted among 68 patients with T2DM attending the Internal Medicine Outpatient Clinic of RSUD Bangil, East Java, Indonesia. Participants were equally divided into DPN (n = 34) and non-DPN (n = 34) groups. DPN was assessed using the Toronto Clinical Neuropathy Scoring System, and serum 25-hydroxyvitamin D [25(OH)D] levels were measured by fluorescence immunoassay. Data were analyzed using the Mann–Whitney test, with $p < 0.05$ considered statistically significant. The median serum vitamin D level was significantly lower in patients with DPN than in those without DPN [15.5 (7.3–44.7) vs. 24.1 (12.3–63.7) ng/mL; $p = 0.001$]. Vitamin D deficiency was more prevalent in the DPN group than in the non-DPN group (76.5% vs. 38.2%; $p = 0.004$). No significant differences were observed in demographic and clinical characteristics between the two groups (all $p > 0.05$). Serum vitamin D levels were significantly lower in patients with DPN than in those without DPN. Vitamin D deficiency was more prevalent in the DPN group.

Keywords: Vitamin D levels, serum 25(OH)D levels, diabetic peripheral neuropathy, type 2 diabetes mellitus.

Introduction

Diabetic neuropathy (ND) is one of the most common chronic complications of diabetes with a reported prevalence of more than 50% in diabetic patients (Pop-Busui et al., 2017). The most prevalent type of neuropathy in individuals with type 2 diabetes mellitus (T2DM) is diabetic peripheral neuropathy (DPN). Longer duration of diabetes, advanced age, poor glycemic control, obesity, hypertension, smoking, and dyslipidemia have all been linked to an increased risk of DPN (Dan Ziegler, 2010; Pop-Busui et al., 2022). DPN has also been linked to vitamin D insufficiency, in addition to these other variables. DPN is 1.22–2.88 times more common in T2DM individuals with vitamin D deficiency than in those with adequate vitamin D levels, according to several studies (Lv et al., 2015; Qu et al., 2017).

It is believed that vitamin D's function in preserving nerve function, lowering inflammation, and offering neuroprotective effects against peripheral nerve damage is connected to diabetic neuropathy. In addition to helping to maintain bone health, vitamin D is a fat-soluble vitamin that acts as a prohormone in a number of bodily metabolic processes. Serum 25-hydroxyvitamin D [25(OH)D] levels are typically used to evaluate vitamin D status since they are the most reliable predictor of the body's vitamin D reserves. Serum 25(OH)D values less than 20 ng/mL (50 nmol/L) are commonly used to indicate vitamin D insufficiency (Sun et al., 2024).

It is well known that vitamin D deficiency raises the incidence of neuropathic pain and contributes to nerve damage in diabetes mellitus (Lv et al., 2015). According to earlier research, patients with diabetic neuropathy had considerably lower vitamin D levels than those without the condition (24.6 ± 11.98 nmol/L vs. 34.74 ± 17.26 nmol/L; $p<0.001$) (Skalli et al., 2012). Additionally, the study revealed that the percentage of patients with vitamin D deficiency was higher in the group with diabetic neuropathy (95%) than in the group without the condition (79.5%; $p<0.05$).

Patients with diabetic neuropathy should have their serum vitamin D levels checked since treating a vitamin D deficit may lessen the severity of the neuropathy (Ghadiri-Anari et al., 2019). Additionally, people with diabetic neuropathic pain have been shown to have better quality of life when taking vitamin D supplements. By 2025, the prevalence of DPN at Bangil Regional General Hospital, a category B hospital in Pasuruan Regency, East Java, is expected to reach 85%. However, data on vitamin D levels in T2DM patients with and without diabetic peripheral neuropathy in Indonesia, particularly at Bangil Regional General Hospital, is still limited. Thus, the purpose of this study was to assess the vitamin D levels of T2DM patients with and without diabetic peripheral neuropathy.

Methods

Research design

This study employed an observational analytical approach with a comparative cross-sectional design. The study was conducted at the Internal Medicine Clinic of Bangil Regional Hospital, Pasuruan Regency, East Java, from February to April 2026, with ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Airlangga University, with certificate number 58/EC/KEPK/FKUA/2026.

Sample

All T2DM patients receiving care at Bangil Regional Hospital's Internal Medicine Clinic during the study period made up the study population. In accordance with the study's criteria, subjects were chosen through successive sampling and split into two groups: T2DM with DPN and T2DM without DPN.

The inclusion criteria for the T2DM with neuropathy study sample were: (1) Age ≥ 18 years; (2) Suffering from T2DM with diabetic peripheral neuropathy; (3) Able to actively communicate and follow instructions; (4) Willingness to participate in the study by signing an informed consent form. The sample for the T2DM without neuropathy study were: (1) Age ≥ 18 years; (2) Suffering from T2DM and not yet experiencing diabetic peripheral neuropathy; (3) Able to actively communicate and follow instructions; (4) Willingness to participate in the study by signing an informed consent form.

The exclusion criteria for this study were: (1) History of amputation; (2) History of chemotherapy; (3) Suffering from ulcers or gangrene of the pedis; (4) Stroke; (5) Chronic kidney disease; (6) Chronic liver disease; (7) Consumption/supplementation of vitamin D; (8) Consumption of phenobarbital, phenytoin, and glucocorticoid drugs. The sample size in this study was determined using the sample size formula for comparative analysis of two unpaired groups with one measurement (Lwanga SK, 1991). The researcher decided to take a research sample of 68 subjects (with a correction factor of 10%), so that each group consisted of 34 subjects.

Data analysis

Statistical analysis was performed using SPSS version 31. Categorical data are presented as frequencies and percentages, while numerical data are presented as mean ± standard deviation or median (minimum–maximum) according to the data distribution. Comparisons between two independent groups were analyzed using the unpaired t-test or the Mann–Whitney test. A p-value <0.05 was considered statistically significant.

Result

This study had 68 participants in total who satisfied the inclusion and exclusion criteria. According to demographic data, the subjects' average age was 56.53 years, and the majority were female (69.1%), had only completed elementary school (48.5%), and were unemployed (55.9%). The majority of participants had diabetes for less than five years (60.3%) and had never smoked (85.3%). The most common pharmacological therapy, according to clinical features, was oral hypoglycemic medicines (ORs) alone (38.2%), followed by insulin alone (27.9%) and a combination of ORs and insulin (33.8%). With a median body mass index of 24.4 kg/m², the majority of participants (73.5%) were overweight or obese. Additionally, 55.9% and 61.8% of participants, respectively, had comorbidities such as dyslipidemia and hypertension. With a mean random blood glucose level of 203.2 mg/dL and a mean HbA1c of 9.7%, the majority of individuals (83.8%) had poor glycemic control. Table 1 displays subject characteristics according to diabetic peripheral neuropathy categories.

Table 1. Neuropathy Group-Based Subject Characteristics

Variable	All Subjects	Without Neuropathy (n = 34)		With Neuropathy (n = 34)		p
		n (%)	Mean ± SD or Median (min - max)	n (%)	Mean ± SD or Median (min - max)	
Age (years)	56.5 ± 10.5		57.1 ± 11.5		55.9 ± 8.3	0.200
Gender						0.115
Male	21 (30.9)	14 (41.2)		7 (20.6)		
Female	47 (69.1)	20 (58.8)		27 (79.4)		
Duration of Diabetes						0.321
< 5 Years	41 (60.3)	23 (67.6)		18 (52.9)		
> 5 Years	27 (39.7)	11 (32.4)		16 (47.1)		

BMI						0.299
Underweight	1 (1.5)	0 (0)		1 (2.9)		
Normal	17 (25.0)	11 (32.4)		6 (17.6)		
Overweight	24 (35.3)	13 (38.2)		11 (32.4)		
Obese I	26 (23.5)	5 (14.7)		11 (32.4)		
Obese II	10 (14.7)	5 (14.7)		5 (14.7)		
Hypertension						0,803
Yes	42 (61.8)	22 (64.7)		20 (58.8)		
No	26 (38.2)	12 (35.3)		14 (41.2)		
LDL-C (mg/dl)	137.3 ± 39.1		132.5 ± 44.1		142.2 ± 33.3	0.200
Total cholesterol (mg/dl)	181.1 ± 44.5		178.3 ± 48.5		183.9 ± 40.5	0.200
Random Blood Glucose (mg/dl)	203.2 ± 76.3		188.5 ± 59.5		218.0 ± 88.5	0.200
HbA1C (%)	9.7 ± 2.6		9.5 ± 2.3		10.0 ± 2.8	0.200
Vitamin D Level	18.7 (7.3 – 63.7)		24.1 (12.3 – 63.7)		15.5 (7.3 – 44.7)	0.001
Deficiency	39 (57.4)	13 (38.2)		26 (76.5)		0.004
Insufficiency	17 (25.0)	11 (32.4)		6 (17.6)		
Sufficiency	12 (17.6)	10 (29.4)		2 (5.9)		

Each group included 34 individuals with and without diabetic peripheral neuropathy, as shown in Table 1. In comparison to the group without diabetic peripheral neuropathy, the group with diabetic peripheral neuropathy had a higher median body mass index and mean levels of LDL cholesterol, total cholesterol, random blood glucose, and HbA1c. However, the group without diabetic peripheral neuropathy had a higher percentage of hypertension. The dyslipidemia prevalence was 55.9% in both groups. All baseline characteristics did not differ significantly between the two groups, according to statistical test results ($p > 0.05$).

The distribution of vitamin D levels indicates that the majority of respondents had deficiencies (57.4%) and insufficiencies (25.0%), resulting in a total of 82.4% of subjects having insufficient vitamin D levels. This suggests that patients with type 2 diabetes mellitus have a high prevalence of hypovitaminosis D.

Discussion

68 patients with type 2 diabetes mellitus were included in this study; they were split equally into groups with and without diabetic peripheral neuropathy. With a mean age of about 56 years, the subjects' demographics generally revealed a preponderance of middle-aged to older people, and most of them were female. This is in line with earlier research showing that aging and hormonal changes in women, particularly during menopause, increase the risk of type 2 diabetes mellitus by impairing glucose metabolism and increasing insulin resistance (Alvina et al., 2023; Kirkman et al., 2012; Mauvais-Jarvis, 2015). In addition, most subjects had low levels of education and were unemployed, which may reflect low health literacy and limitations in managing chronic diseases, as has been reported in several previous studies (Alvina et al., 2023; Ariza et al., 2025; Safitri et al., 2024).

The majority of patients had poor glycemic control, were overweight or obese, and had a comparatively high incidence of hypertension and dyslipidemia, according to the clinical features of the individuals. Through processes like insulin resistance, oxidative stress, chronic inflammation, and microvascular damage, these factors are known to contribute to the pathophysiology of type 2 diabetes mellitus and diabetic peripheral neuropathy (Bader et al., 2025; Dan Ziegler, 2010; Fentie et al., 2023; Franceschi & Campisi, 2014; Hamida et al., 2021; Ismail, 2014; Pop-Busui et al., 2022). Age, gender, smoking history, duration of diabetes, body mass index, hypertension, dyslipidemia, and glycemic control did not significantly differ between the groups with and without neuropathy, according to the analysis ($p > 0.05$). These results show that these factors did not function as significant confounders in this investigation because both groups had comparatively similar baseline characteristics.

The interpretation that the variations in vitamin D levels are more likely associated with the existence of diabetic peripheral neuropathy than with traditional demographic or metabolic parameters is supported by the homogeneity of the two groups' features. As a result, there is comparatively less chance of bias resulting from variations in baseline features when evaluating the relationship between vitamin D levels and diabetic peripheral neuropathy in this study. All participants in this study had a median vitamin D level of 18.6 ng/mL, with a range of 7.35–63.74 ng/mL. 82.4% of the sample population had low vitamin

D levels, with most participants (57.4%) being categorized as deficient and 25.0% as insufficient. This study's significant frequency of hypovitaminosis D is in line with other research that show a 60–90% incidence of vitamin D deficiency in patients with type 2 diabetes mellitus (Nasr et al., 2022; Vijay et al., 2023). These results imply that even among populations residing in tropical regions with comparatively high levels of solar exposure, vitamin D deficiency is still a prevalent issue among individuals with type 2 diabetes mellitus.

Sub-analyses of a number of subject characteristics, such as age, gender, occupation, exercise habits, sun exposure, body protection use, and body mass index, revealed no significant differences between vitamin D status or levels and these variables ($p > 0.05$). This suggests that low vitamin D levels in the study population are probably impacted by other variables not examined in this study, such as daily physical activity, consumption of foods high in vitamin D, and the length and intensity of sun exposure. Decreased vitamin D synthesis in the skin is known to be influenced by sunscreen use, increased skin pigmentation, decreased 7-dehydrocholesterol levels due to aging, and a lifestyle that tends to avoid sun exposure through the use of closed clothing or body protection (Chalcraft et al., 2020; Progress & Holick, 2007). In addition, vitamin D requirements are also difficult to meet only through food intake because natural sources of vitamin D are relatively limited (Bruins & Létinois, 2021). Therefore, vitamin D deficiency can still be found in populations living in tropical regions.

According to the study's findings, the group with diabetic peripheral neuropathy had a median vitamin D level of 15.5 ng/mL (7.3–44.7), which was lower than the group without the condition, which had a median level of 24.1 ng/mL (12.3–63.7). Patients with type 2 diabetes mellitus who had diabetic peripheral neuropathy had lower vitamin D levels than those without neuropathy, according to the Mann-Whitney test, which showed that this difference was statistically significant ($p = 0.001$). These findings support the idea that vitamin D contributes to the pathophysiology of neuropathic complications in diabetes since they are in line with a number of earlier studies that found a link between vitamin D deficiency and an increased incidence of diabetic peripheral neuropathy (Karonova et al., 2020).

Analysis by vitamin D category also showed a similar pattern. The proportion of patients with vitamin D deficiency was higher in the diabetic peripheral neuropathy group than in the group without neuropathy, while the proportion of patients with sufficient vitamin D levels was higher in the group without neuropathy. This difference in the distribution of vitamin D categories was statistically significant ($p = 0.004$), indicating that the lower the vitamin D level, the higher the proportion of diabetic peripheral neuropathy cases. These findings support the hypothesis that vitamin D status is a factor associated with the development of diabetic peripheral neuropathy and is a potentially modifiable risk factor..

Numerous neuroprotective molecular pathways are known to be connected to vitamin D's action in diabetic peripheral neuropathy. It is well known that vitamin D increases the expression of nerve growth factor (NGF), modulates the inflammatory response by lowering proinflammatory cytokines, and lessens oxidative stress, all of which contribute to peripheral nerve injury (Karonova et al., 2020; Lv et al., 2015; Tang et al., 2025). Furthermore, vitamin D contributes to the preservation of neuronal calcium homeostasis and mitochondrial activity, both of which are critical for the integrity and regeneration of nerve fibers (Tang et al., 2025). The development of diabetic peripheral neuropathy can be accelerated by vitamin D deficiency because it can lead to decreased activation of the vitamin D receptor (VDR), impaired nerve regeneration, and increased susceptibility of neurons to injury owing to chronic hyperglycemia and persistent inflammation.

The individuals' baseline characteristics were comparatively similar, as seen by the lack of significant variations in age, gender, smoking history, duration of diabetes, body mass index, hypertension, dyslipidemia, or glycemic control between the two groups. Our condition supports the hypothesis that traditional metabolic factors believed to be involved in the pathophysiology of neuropathy did not significantly affect the connection between vitamin D levels and diabetic peripheral neuropathy in our investigation. Table 2 compares vitamin D levels by group among patients with diabetic peripheral neuropathy and other studies.

Table 2. Comparative analysis of vitamin D levels with other studies

Studies	Without Neuropathy		With Neuropathy		p
	%	Mean ± SD or Median (min - max)	%	Mean ± SD or Median (min - max)	
This Study:					
Vitamin D level (ng/mL)		24.1 (12.3 – 63.7)		15.5 (7.3 – 44.7)	0.001
Deficiency	38.2		76.5		
Shehab et al. (2012) :					
Vitamin D level (ng/mL)		23.3 ± 23.6		14.8 ± 15.9	0.001
Deficiency	28.0		50.0		
Rahaman et al. (2023) :					
Vitamin D level (ng/mL)		18.6 (11.2 – 22.6)		11.8 (9.1 – 18.1)	0.006
Deficiency	60.4		81.4		

The findings of the comparative test indicated that the two groups differed statistically significantly ($p < 0.05$). This finding indicates a significant difference in vitamin D levels between the groups with and without diabetic peripheral neuropathy. These results are in consistent with a study by Shehab et al. (2012), which found that patients with neuropathy had

significantly lower vitamin D levels (14.8 ± 15.9 ng/mL) than patients without neuropathy (23.3 ± 23.6 ng/mL), and that the neuropathy group had a significantly higher prevalence of vitamin D deficiency (50% vs. 28%; p = 0.001) (Shehab et al., 2012). In a similar vein, Rahaman et al. (2023) discovered that patients with neuropathy had lower vitamin D levels (median 11.8 ng/mL) than patients without neuropathy (median 18.6 ng/mL), along with a greater prevalence of deficiency (81.4% vs. 60.4%; p = 0.006) (Rahaman et al., 2023).

The results of this study and other research consistently show that patients with type 2 diabetes mellitus (T2DM) and diabetic peripheral neuropathy (DPN) had considerably lower serum vitamin D [25(OH)D] levels than patients without neuropathy. Although a causative relationship cannot be proven based on cross-sectional research, these consistent findings further support the association between vitamin D insufficiency and diabetic peripheral neuropathy in patients with type 2 diabetes. According to the study's findings, vitamin D level testing may be included in a thorough assessment of patients with type 2 diabetes mellitus, particularly those who are at risk for diabetic peripheral neuropathy. Finding and treating vitamin D deficiency has the potential to be an additional tactic in avoiding or slowing the onset of diabetic peripheral neuropathy because it is a controllable factor.

Conclusion

Compared to the group without neuropathy, patients with type 2 diabetes mellitus and diabetic peripheral neuropathy had considerably lower vitamin D levels and greater rates of deficiency. The evidence that vitamin D status is linked to neuropathic problems is strengthened by the same baseline features of both groups, which may be utilized for early risk assessment. However, given the limitations of this study's cross-sectional methodology, additional prospective research is required to confirm the causal association and advantages of vitamin D therapy.

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