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Association of Vitamin D Level and Nerve Conduction Study Parameters with Cognitive Function in Diabetic Neuropathy Patients

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Abstract

BACKGROUND: Type 2 diabetes mellitus (T2DM) and its major long-term complication, diabetic polyneuropathy (DPN), continue to be a major global health problem and are important contributors of significant disability worldwide. Vitamin D plays a significant role in their pathogenesis as well as in the development of dementia in non-diabetic patients. Nevertheless, the role of Vitamin D in the development of cognitive impairment in DPN patients has not yet been extensively studied.

AIM: We aimed to investigate the association between Vitamin D level and cognitive function in DPN patients and to evaluate several potential contributor factors to cognition, including demographic factors, glycemic control, and nerve conduction study (NCS) parameters.

METHODS: Thirty-one DPN patients were included in this cross-sectional study. Patients were recruited from the outpatient endocrinology and neurology clinic of Haji Adam Malik General Hospital Medan Indonesia. We used the diabetic neuropathy examination (DNE) scale, diabetic neuropathy symptom (DNS) scale, and NCS to determine the presence and severity of the neuropathy. We measured the levels of Vitamin D, random blood sugar, and glycated hemoglobin (HbA1c). Cognitive function was assessed using the Indonesian version of Montreal Cognitive Assessment (MoCA-INA), trail making test A and B (TMT A and TMT B), and verbal fluency test.

RESULTS: Most of the patients were female (80.6%), with a mean age of 55.71 ± 8.34 years. The proportion of patients with abnormal cognitive function was higher than cognitively unimpaired patients. The mean of MoCA-INA score and level of Vitamin D was lower than normal, 23.32 ± 3.00 and 24.91 ± 13.59 ng/ml, respectively. Using the Pearson correlation test, we did not find any significant association of Vitamin D level, NCS parameters, and other clinical characteristics with global cognitive function. Age and level of education were significantly associated with MoCA-INA score. Blood sugar level was significantly higher in patients with normal TMT-A and TMT-B tests compared to patients with abnormal results.

CONCLUSION: Vitamin D and NCS parameters are not associated with cognitive function. Of the demographic and clinical characteristics, a significant association exists between age, level of education, and blood sugar level and cognition. This might suggest the complexity underlying cognitive impairment in T2DM patients.

Introduction

Type 2 diabetes mellitus (T2DM) remains a major health problem worldwide. It is estimated that about 1 in 11 adults have diabetes mellitus globally. Asia is a major area of this rapidly emerging T2DM global epidemic [1]. T2DM and its complications are among the major causes of reduced life expectancy and increased disability worldwide [2]. The most common complication of diabetes mellitus (DM), as well as the most disabling one, is diabetic neuropathy (DN), especially diabetic polyneuropathy (DPN) that may affect up to 60% DM patients at the time of diagnosis [3]. Careful neurologic examinations are important in the early detection of DPN and nerve conduction studies (NCS) play a crucial role in detecting neural changes even before the sign develops [4]. Cognitive impairments are also prevalent in diabetic patients and significantly affect the quality of life of patients and their caregivers and pose significant clinical challenges [5]. The prevalence of dementia is higher in diabetic patients than non-diabetic subjects [6].

Recently, a growing body of literature suggests an important pathogenetic role of Vitamin D in both T2DM and DPN. Vitamin D plays important roles in the metabolism of glucose, affects calcium handling in beta cells of pancreas, thereby affecting insulin synthesis and secretion from pancreatic beta- cells, and it also improves insulin sensitivity in peripheral muscle and fats cells [7], [8], [9]. Vitamin D has also been reported to be involved in the modulation of inflammation and oxidative stress [10], [11], [12] and glycemic control in

T2DM [13]. Vitamin D deficiency is related to the higher incidence of T2DM [14], worsening insulin resistance that subsequently leads to the development of T2DM [15], [16], [17], and also related to DPN symptoms [18], [19], [20]. It is now considered as an important nutritional risk factor in T2DM. Therefore, several authors have favored supplementation with Vitamin D to improve the symptoms of sensory-motor neuropathy [21], [22], [23].

Vitamin D and its metabolites are involved in various neuroprotective mechanisms related to nerve growth factors and vasoprotection that contribute to better cognition [24], [25]. Several previous studies examining the role of Vitamin D in cognition have yielded various results [26], [27], [28], [29], [30] and study about the role of Vitamin D in cognitive function, specifically in diabetic patients is still limited, with one only randomized control trial examining effects of Vitamin D supplementation and found no significant differences in cognitive outcomes [31]. The factors contributing to cognitive impairment in T2DM patients are numerous, including the intrinsic pathophysiology of T2DM itself, the glycemic control, the existence of other comorbid, such as retinopathy, neuropathy, and other factors not directly related to T2DM, such as age and education that more likely reflect the cognitive reserve [29], [30], [31].

This study aimed to investigate the association between Vitamin D level and cognitive function in DPN patients and to evaluate several potential contributor factors to cognition, including demographic factors, glycemic control, and nerve conduction study (NCS) parameters.

Methods

Study population

Thirty-one outpatients with T2DM and diabetic neuropathy were sequentially evaluated in the outpatient endocrinology and neurology clinic of Haji Adam Malik General Hospital Medan Indonesia from January to March 2019. We included all DPN patients who were literate and used Bahasa Indonesia as their formal language and had given consent to be included in the study. We excluded patients with impaired renal or liver function or had been previously diagnosed with dementia, stroke, or other neurological and major psychiatric disorders. This study was approved by the Local Ethical Committee and written informed consent was obtained from each patient. We collected data and detailed medical history from the patients such as sex, age, duration of DM, smoking status, type and number of anti-diabetic drugs, and the presence of the metabolic syndrome. Glycated hemoglobin (HbA1c) level was measured using the enzyme immunoassay method, and serum vitamin 25 (OH) D status was evaluated using the chemiluminescent immunoassay method.

Neuropathy assessment

For the assessment of neuropathy, we used Diabetes Neuropathy Symptoms (DNS) and Diabetic Neuropathy Examination (DNE) scales. The DNS score ≥1 was considered neuropathy and DNE score >3 was significant for the presence of neuropathy [32]. All patients underwent NCS examination by the same neurologist using Cadwell ENMG (electroneuromyography) machine to determine the presence and severity of DPN. NCS consisted of distal latencies (DL), amplitude (A), and nerve conduction velocity (NCV).

Cognitive function assessment

Cognitive function was assessed using the Indonesian Version of Montreal Cognitive Assessment (MoCA-INA), trail making test A and B (TMT A and TMT B), and verbal fluency tests (VFT-animals). The MoCA assesses several cognitive domains, including executive function, visuospatial function, attention and concentration, memory, language, calculation, and orientation [33]. The Indonesian version of MoCA, namely MoCA-INA, has been developed and validated in Indonesia and has been extensively used to assess cognitive function in various populations. The maximal score is 30, with score <26 indicates cognitive impairment [34].

Trails making test is a neuropsychological test of visual attention, scanning and visuomotor tracking, divided attention, and cognitive flexibility. It was given in two parts, A and B. Both parts of the trail making test consist of 25 circles distributed over a sheet of paper. In Part A, the circles were numbered 1–25, and the patients were asked to draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1–13) and letters (A–L); as in Part A, the patients were asked to draw lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). The patients were instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. If the patient made an error, we pointed it out immediately and allowed the patient to correct it. Errors affected the patient's score only in that the correction of errors was included in the completion time for the task. Results for both TMT A and B were recorded as the number of seconds required to complete the task; therefore, higher scores reveal greater impairment and the tests were considered abnormal if the patient had not completed TMT A and TMT B after 3 and 5 min had elapsed, respectively.

Verbal fluency refers to the ability to produce spontaneous speech fluently without undue word-finding pauses or failures in word searching. In

VFT-animal naming test, we instructed the patient to recall and name as many animals as possible within 60 s. The score was the number of correctly produced animal names during that 60 s. The normal range of score was 18–22 animal names, with score < 18 was considered abnormal [35], [36], [37].

Statistical analysis

The demographic data were presented as mean or frequency, as appropriate. The NCS parameters were expressed as mean ± standard deviation. Pearson's correlation analysis was performed to determine the relationships between variables. The statistical difference between groups was analyzed using an independent t-test. For parametric variables, data were presented as mean ± standard deviation (SD) and nonparametric variables were presented as median (minimal–maximal). Pearson test was used for correlation analysis. The results were considered significant at $p < 0.05$. Statistical analysis was performed with a computerized program.

Results

There were 31 DPN patients that included in this study, consisted of more female (80.6%) than male (19.4%) patients. The mean age was 55.71 ± 8.34 years. Most patients were non-smoker (93.5%) and had concurrent metabolic syndrome (64.5%). The mean duration of DM was 6.48 ± 4.86 years. The mean level of Vitamin D was 24.91 ± 13.59 ng/ml. Cognitive assessment showed that 51.6% had abnormal MoCA-INA score, and the mean score was 23.32±3.00. The detailed subject characteristics are presented in Table 1.

Assessment of neuropathy using NCS study showed that mean NCV of motor median, ulnar, peroneal, and tibial nerves were normal. Mean NCV of sensory median, ulnar, and sural nerves were decreased. Mean A of motor median and peroneal nerves were decreased. Mean A of sensory median, ulnar, and sural nerves were decreased. Mean DL of motor median nerve was increased. Mean DL of the sensory median, ulnar, and sural nerves were normal. From these results, axonal degeneration was more dominant as the main pathological mechanism of DN (Table 2).

To analyze the association between variables and MoCA-INA score, we used Pearson correlation test and found a significant correlation only between age and level of education and MoCA-INA score. There was no significant correlation between other demographic factors and NCS parameters and MoCA-INA score (Table 3).

Table 1: Subject characteristics

Variable	Number	Percentage
Age, mean±SD (years)	55.71 ± 8.34	
Sex		
Male	6	19,4
Female	25	80,6
Level of education		
Elementary	1	3.2
Junior high school	1	3.2
Senior high school	8	25.8
College/University	21	67.7
Smoking status		
Yes	2	6,5
No	29	93.5
Metabolic syndrome		
Yes	20	64.5
No	11	35.5
Duration of DM, mean±SD (years)	6.48 ± 4.86	
Number of anti-diabetic drug		
0	1	3.2
1	19	61.3
>1	11	35.5
Type of anti-diabetic drug		
None	1	3.2
Insulin	15	48.4
Oral	14	45.2
Combination	1	3.2
DNS, median (min–max)	2 (1–3)	
DNE, median (min–max)	4 (1–13)	
Random blood sugar level, mean±SD (mg/dl)	231.52 ± 24.67	
HbA1c, mean±SD (%)	8.97 ± 2.22	
Level of Vitamin D, mean±SD (ng/ml)	24.91 ± 13.59	
MoCA-INA, mean±SD	23.32 ± 3.00	
MoCA-INA		
Normal (≥26)	15	48.4
Abnormal (<26)	16	51.6
Verbal fluency test		
Normal	15	48.4
Abnormal	16	51.6
Trail making test A		
Normal	16	51.6
Abnormal	15	48.4
Trail making test B		
Normal	17	54.8
Abnormal	14	45.2

Pearson correlation test

We also compared the differences of these variables based on the results of TMT-A, TMT-B, and verbal fluency test and found significant differences on blood sugar level based on TMT-A and TMT-B tests and difference of DNS based on TMT-A test (Table 4).

Discussion

In the past few decades, T2DM and its complications have reached epidemic levels and posed a major global health concern, particularly in developing countries [1]. Diabetic polyneuropathy (DPN) is one of the most common complications of T2DM and related to increased disability [3]. A growing body of evidence has shown the role of Vitamin D in T2DM and DPN pathogenesis, including inflammation and oxidative stress [8], [9], [10], [11], [12]. In this study, we found a lower level of Vitamin D in DPN patients (24.91 ± 13.59 ng/ml), which the adequate level of Vitamin D is ≥30 ng/ml [18]. This is in line with a finding from one meta-analysis that found in Asian, diabetic patients with Vitamin D deficiency are 1.22 times more likely to suffer from DPN compared with people with normal

Table 2: Nerve conduction studies results

Nerve	Motor NCV (m/s)	Sensory NCV (m/s)	Motor amplitude (mV)	Sensory amplitude (mV)	Motor distal latency (ms)	Sensory distal latency (ms)
Median	48.13 ± 7.27	25.23 ± 20.91	3.71 ± 2.17	8.33 ± 11.91	5.25 ± 1.78	2.48 ± 2.09
Ulnar	51.45 ± 5.43	40.90 ± 15.56	5.37 ± 1.74	14.38 ± 11.23	2.97 ± 0.64	2.82 ± 1.23
Peroneal	41.29 ± 9.62	NA	1.78 ± 1.07	NA	4.99 ± 1.49	NA
Tibial	38.90 ± 10.29	NA	7.52 ± 4.55	NA	3.48 ± 1.03	NA
Sural	NA	14.48 ± 18.81	NA	3.01 ± 4.23	NA	1.43 ± 1.90

NA: Not applicable.

Table 3: Correlation between subject characteristics, Vitamin D level, and NCS parameters with MoCA-INA score

Variable	MoCA-INA
Age	**p=0.024**
	r = −0.404
Level of education	**p=0.029**
	r=0.392
DNS	p=0.245
	r = −0.215
DNE	p=0.197
	r = −0.238
Blood sugar level	p=0.069
	r= −0.331
HbA1c	p=0.843
	r = −0.037
Vitamin D level	p=0.669
	r=0.080
Motor median NCV	p=0.758
	r=0.058
Motor ulnar NCV	p=0.875
	r=0.030
Sensory median NCV	p=0.552
	r = −0.111
Sensory ulnar NCV	p=0.399
	r = −0.157
Motor peroneal NCV	p=0.193
	r=0.240
Motor tibial NCV	p=0.840
	r=0.038
Sensory sural NCV	p=0.720
	r = −0.067
Motor median amplitude	p=0.102
	r=0.299
Motor ulnar amplitude	p=0.573
	r=0.105
Sensory median amplitude	p=0.609
	r = −0.096
Sensory ulnar amplitude	p=0.477
	r = −0.132
Motor peroneal amplitude	p=0.529
	r=0.117
Motor tibial amplitude	p=0.704
	r = −0.071
Sensory sural amplitude	p=0.822
	r = −0.042
Motor median DL	p=0.323
	r=0.184
Motor ulnar DL	p=0.781
	r=0.052
Sensory median DL	p=0.720
	r= −0.067
Sensory ulnar DL	p=0.085
	r= −0.315
Motor peroneal DL	p=0.289
	r=0.197
Motor tibial DL	p=0.395
	r=0.158
Sensory sural DL	p=0.505
	r = −0.124

Pearson correlation test. p <0.05

Vitamin D level [20]. Vitamin D deficiency has also been reported to exacerbate symptoms of painful DN [18] and associated with self-reported peripheral neuropathy symptoms even after adjusting for demographic factors, obesity, co-morbidities, use of medications for neuropathy, and diabetes duration and control [19]. Several studies have suggested supplementation with Vitamin D to improve the symptoms of sensory-motor neuropathy [21], [22], [23].

Vitamin D level has been shown to have a significant negative association with glycemic control (HbA1c level) [13]. We did not analyze this association in our study, but we found a higher of HbA1c level (8.97 ± 2.22%) compared to the normal reference value of <6.5% [38], and high blood sugar level (231.52 ± 24.67 mg/dl) showing that T2DM patients in our study had poor glycemic control. These conditions might have contributed to the development of DPN since the major risk factors of DPN include diabetes duration, hyperglycemia, and age, followed by prediabetes, hypertension, dyslipidemia, and obesity [39].

TD2M may also affect cognition. The MoCA-INA score in our study was lower (23.32 ± 3.00) than normal (≥26). The proportion of patients with abnormal global cognitive function in our study was also higher than cognitively unimpaired patients. It is well recognized that the prevalence of dementia and cognitive impairment is higher in diabetic patients than non-diabetic subjects. Diabetes in midlife is associated with a 19% greater cognitive decline over 20 years compared to those without diabetes [40]. The underlying mechanisms linking diabetes and cognitive dysfunction include advanced protein glycation and oxidative stress related to glucose toxicity and insufficient insulin action, atherosclerosis, and microvascular disease as a result of insidious ischemia. The aging and genetic factors may be also involved in the development of dementia in diabetic patients [5], [6].

Cognitive impairment may be related to DPN in T2DM patients as they may share similar multiple pathogenic pathways, such as inflammation, oxidative stress, and dyslipidemia, among others [41]. Our study found did not find a significant association between NCS parameters with MoCA-INA score. This is similar to the finding from Moreira *et al*. (2015) that found no differences between patients with and without PDN in all cognitive tests ($p > 0.05$ in all comparisons).

Vitamin D (25-hydroxy Vitamin D [25(OH)D]) is a steroid hormone with a variety of physiological roles other than its well-known role in calcium homeostasis. Currently, there is an emerging role of Vitamin D in cognition. There was not a significant association between Vitamin D and global cognitive function as measured by MoCA-INA in this study. Several previous studies examining the role of Vitamin D in cognition have yielded various results. Among individuals without diabetes, there is a significant association between low serum Vitamin D level and poorer cognitive function and a higher risk of Alzheimer's Disease [26] and increased risk of all-cause dementia [27], [28]. One study found improvement in cognitive function after Vitamin D supplementation in females with low Vitamin D level [28]. However, one large cohort study reported that

Table 4: Differences of subject characteristics, Vitamin D level, and NCS parameters based on cognitive function

Variable	TMT A		p	TMT B		p	Verbal fluency		p
Mean ± SD	Normal	Abnormal		Normal	Abnormal		Normal	Abnormal	
Age	54.06 ± 7.03	57.47 ± 9.48	0.268	54.18 ± 6.82	57.57 ± 9.83	0.476	55.40 ± 6.89	56.00 ± 9.74	0.751
DNS	1 (1–3)	2 (1–3)	**0.025**	1 (1–3)	2 (1–3)	0.086	1 (1–3)	2 (1–3)	0.536
DNE	4 (1–10)	5 (3–13)	0.255	4 (1–12)	4 (3–13)	0.561	4 (1–12)	4 (1–13)	0.743
Blood sugar level (mg/dl)	222.13 ± 24.7	241.53 ± 20.99	**0.032**	223.18 ± 24.3	241.64 ± 21.7	**0.043**	223.60 ± 25.7	238.94 ± 21.8	0.095
HbA1c (%)	8.90 ± 2.46	9.04 ± 2.01	0.869	8.84 ± 2.40	9.13 ± 2.05	0.710	8.42 ± 1.56	9.48 ± 2.64	0.158
Vitamin D level (ng/ml)	22.38 ± 12.99	27.60 ± 14.16	0.297	22.63 ± 12.62	27.67 ± 14.69	0.343	24.75 ± 13.37	25.05 ± 14.24	0.950
Motor median NCV (m/s)	47.31 ± 8.24	49.00 ± 6.22	0.662	47.59 ± 8.06	48.79 ± 6.39	0.656	48.73 ± 5.86	47.56 ± 8.53	0.662
Motor ulnar NCV (m/s)	51.31 ± 5.92	51.60 ± 2.07	0.960	51.24 ± 5.74	251.71 ± 5.24	0.812	51.40 ± 5.08	51.50 ± 5.91	0.960
Sensory median NCV (m/s)	25.75 ± 21.18	24.67 ± 21.35	0.619	24.24 ± 21.44	26.43 ± 20.99	0.777	27.20 ± 20.57	23.38 ± 21,73	0.619
Sensory ulnar NCV (m/s)	41.88 ± 13.76	39.87 ± 17.71	0.709	39.41 ± 16.75	42.71 ± 14.38	0.565	39.80 ± 16.85	41.94 ± 14.73	0.709
Motor peroneal NCV (m/s)	41.75 ± 5.48	40.80 ± 12.86	0.618	41.29 ± 5.63	41.29 ± 13.21	0.998	42.20 ± 5.59	40.44 ± 12.42	0.618
Motor tibial NCV (m/s)	40.31 ± 5.89	37.40 ± 13.60	0.463	40.00 ± 5.84	37.57 ± 14.09	0.522	40.33 ± 5.49	37.56 ± 13.39	0.463
Sensory sural NCV (m/s)	11.50 ± 17.85	17.67 ± 19.89	0.974	10.82 ± 17.50	18.93 ± 20.01	0.239	14.60 ± 18.75	14.38 ± 19.48	0.974
Motor median amplitude (mV)	3.83 ± 2.02	4.77 ± 1.15	0.668	3.72 ± 1.99	3.69 ± 2.45	0.970	3.89 ± 1.75	3.54 ± 2.55	0.668
Motor ulnar amplitude (mV)	5.33 ± 1.26	2.97 ± 0.75	0.914	5.31 ± 1.22	5.45 ± 2.26	0.833	5.41 ± 1.29	5.34 ± 2.12	0.914
Sensory median amplitude (mV)	7.48 ± 11.79	2.34 ± 2.06	0.830	7.04 ± 11.57	9.91 ± 12.55	0.513	7.85 ± 11.99	8.79 ± 12.19	0.830
Sensory ulnar amplitude (mV)	12.85 ± 11.01	2.57 ± 1.19	0.628	12.09 ± 11.10	17.16 ± 11.15	0.217	13.35 ± 11.74	15.35 ± 11.03	0.628
Motor peroneal amplitude (mV)	1.96 ± 0.67	5.01 ± 2.05	0.990	1.87 ± 0.74	1.67 ± 1.39	0.624	1.78 ± 0.77	1.78 ± 1.32	0.990
Motor tibial amplitude (mV)	746 ± 3.26	3.50 ± 1.36	0.820	7.08 ± 3.53	8.06 ± 5.66	0.557	7.72 ± 3.98	7.34 ± 5.16	0.820
Sensory sural amplitude (mV)	2.46 ± 4.01	1.73 ± 1.99	0.950	2.32 ± 3.93	3.85 ± 4.58	0.324	3.06 ± 4.14	2.96 ± 4.45	0.950
Motor median DL (ms)	5.70 ± 2.15	4.77 ± 1.15	0.280	5.72 ± 2.09	4.69 ± 1.14	0.109	5.61 ± 2.19	4.91 ± 1.26	0.280
Motor ulnar DL (ms)	2.97 ± 0.56	2.97 ± 0.75	0.790	2.97 ± 0.54	2.96 ± 0.78	0.979	3.00 ± 0.50	2.94 ± 0.77	0.790
Sensory median DL (ms)	2.61 ± 2.19	2.34 ± 2.06	0.425	2.45 ± 2.21	2.51 ± 2.03	0.944	2.79 ± 2.15	2.18 ± 2.06	0.425
Sensory ulnar DL (ms)	3.06 ± 1.25	2.57 ± 1.19	0.485	2.88 ± 1.42	2.76 ± 1.00	0.793	2.66 ± 1.18	2.98 ± 1.29	0.485
Motor peroneal DL (ms)	4.96 ± 0.73	5.01 ± 2.05	0.963	5.02 ± 0.75	4.94 ± 2.10	0.893	5.00 ± 0.73	4.98 ± 1.98	0.963
Motor tibial DL (ms)	3.46 ± 0.63	3.500 ± 1.36	0.809	3.51 ± 0.64	3.45 ± 1.39	0.883	3.43 ± 0.59	3.53 ± 1.33	0.809
Sensory sural DL (ms)	1.16 ± 1.84	1.73 ± 1.99	0.731	1.09 ± 1.79	1.85 ± 2.00	0.279	1.56 ± 2.05	1.32 ± 1.82	0.731

T-independent test p <0.05.

cognition was not affected by Vitamin D level alone but also population and sociological variables, and found no statistically significant association between Vitamin D and cognitive function in the elderly population [30]. Our study also found a significant association between age and education with cognitive function that might suggest that these factors were more closely related to cognition compared to other factors.

The best neuropsychological tests to evaluate impaired cognition in diabetes have not been established. The Montreal Cognitive Assessment is a screening test that is often performed in a clinical setting. More in-depth testing involves an in-depth evaluation of multiple cognitive domains as cognitive impairment in diabetic patients may affect several domains [42]. We used several cognitive examination tools to evaluate cognition more detailed and provide a better evaluation. We found significantly higher blood sugar level in the group of patients with abnormal TMT A and TMT B results that reflected impairment in attention and executive function (set-shifting, mental flexibility, and processing speed). Several previous studies have shown deficits in different cognitive domains in diabetic patients, including reduced performance in information processing speed and impaired memory, attention, and executive function. Compared to matched controls, T2DM subjects had significantly lower scores in the trail making test B, color-word Stroop test, semantic fluency, and digit-symbol modalities test [43], [44], [45].

In summary, although T2DM patients in our study showed lower cognitive scores compared to standard reference norms, this impairment did not seem related to the presence and severity of the DPN, the level of Vitamin D, other demographic and clinical factors other than age, education, and blood sugar level. This finding might reflex the complexity in the underlying mechanism of diabetic neuropathy in T2DM because there are many potential contributing factors. It also emphasizes the need for further studies to clarify the factors influencing cognitive impairment in diabetic patients that can lead to better management and quality of life.

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