Original Article

Impact Of Vitamin D Level On Diabetic Patients With Peripheral Neuropathy: An Analytical Cross-Sectional Study

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Abstract

Aim: This study evaluates the relationship between the occurrence of diabetic neuropathy in diabetic individuals and the effect of vitamin D levels in them. This study also evaluates whether there is an association with specific subtypes of diabetic neuropathy.

Study design: An analytical cross-sectional study

Place and Duration: This study was conducted at Shaheed Mohtarma Benazir Bhutto Medical College Lyari Karachi from June 2021 to July 2022.

Methodology: Overall, 84 type 2 diabetes mellitus individuals were involved in this research. These 84 patients were divided into 4 groups, each having an equal number of patients. These groups were patients (A) with severe pain in diabetic neuropathy, (B) with no pain neuropathy, (C) with no pain neuropathy but having neuropathic ulcers, and (D) without neuropathy. The clinical examination as well as the neurological examination was done for all patients. They also went under nerve conduction study. The level of vitamin D and complete blood count were evaluated in these groups.

Results: Group A (with severe pain due to diabetic neuropathy) had 71% of patients who had lower levels of vitamin D. The level of vitamin D ranged from 5.2-41 nanograms/dl and the mean was 17.6. Group B (with no pain neuropathy) had 61% of patients who had lower levels of vitamin D. The level of vitamin D ranged from 6.4-36.5 nanograms/dl and the mean was 19. Group D (without neuropathy) had only 6% of patients who had vitamin D deficiency. A negative correlation was seen between the neuropathy score and vitamin D level. The lesser the level of vitamin D, the more the neuropathy score.

Conclusion: Vitamin D levels were reported to be lesser in those individuals who had diabetic neuropathy, and significantly in those who had severe pain due to diabetic neuropathy.

Keywords: Diabetes, neuropathy, vitamin D, adults

Introduction

Diabetes mellitus occurs when there is a defect in insulin secretion or there is a problem in the functioning of insulin, it is a metabolic disease, which is a worldwide health concern. According to the WHO, around 415 million human beings around the world are affected with diabetes and the WHO expects it to reach 643 million in 2040 [1]. This shows that diabetes is a common health concern and will continue to grow. Around fifty percent of patients who are affected with diabetes mellitus have diabetic peripheral neuropathy, which is a common problem that is associated with diabetes mellitus. One of the major sources of mortality and morbidity is diabetic peripheral neuropathy because about 11% of patients with diabetic peripheral neuropathy face symptoms that are chronic and painful, which automatically affect their lives [2].

The pathophysiology of diabetic peripheral neuropathy is currently not recognized, and there are no globally acknowledged cures for diabetic peripheral neuropathy. Therefore, the focus of surgery is symptom control with medication, which has finite efficacy and frequently has considerable side-effects that limit its usage [3]. It has been found in prior research that hyperglycemia, duration of the disease, obesity, elevated glycated hemoglobin, and elevated albumin excretion rates are the factors that are related to the occurrence of diabetic peripheral neuropathy. But there is still a blurred image of the pathological progress of diabetic peripheral neuropathy. Thus, there may be other risk factors which would be linked to the development diabetic peripheral neuropathy that are still needed to be assessed [3]. Vitamin D is said to be a steroid hormone that affects the human body extensively. Vitamin D helps in the adjustment of bone metabolism as well as other metabolic processes. However, it was found in a study that autoimmune disease is strongly associated with serum vitamin D levels [4].

With 1-25-OH vitamin D consumption, diabetes can be delayed. Other studies evaluate the etiology and development of type 2 diabetes mellitus, as well as the development of complications that are microvascular and are caused by the deficiency of vitamin D [5]. It was also seen that some studies described the relation between diabetic peripheral neuropathy and serum vitamin D levels. In this research, we measured serum vitamin D levels in individuals with diabetes with various forms of diabetic peripheral neuropathy to examine vitamin D's role as a possible risk factor, which would lead to improved disease treatment.

Therefore, this research evaluates the relationship between the occurrence of diabetic neuropathy in diabetic patients and the effect of vitamin D levels in them. This study also evaluates whether there is an association with specific subtypes of diabetic neuropathy.

Methodology

This study includes a total of 84 patients with type 2 diabetes mellitus with respect to the World Health Organization criteria. The patients who were alcoholics, who had non-diabetic neuropathies, who had certain disorders such as renal or hepatic failure and those who were highly dosed with vitamin D supplements were not included in this study.

Overall, 84 individuals with diabetes were involved in this research. These 84 patients were divided into 4 groups, each having an equal number of patients (21 patients). These groups were having patients (A) with severe pain in diabetic neuropathy (ten males and eleven females), (B) with no pain neuropathy (ten males and eleven females), (C) with no pain neuropathy but having neuropathic ulcers (ten males and eleven females), and (D) without neuropathy (six males and fifteen females). Every patient was involved in activities that were exposed to sunlight. Almost all of the patients live in areas that were sunny and many of them were picked during hot seasons.

Every patient's medical history was recorded in detail. The medical history contained information related to the time span and control of diabetes, their record of vitamin D supplementation, and their hypoglycemic medications. Toronto clinical scoring system (TCSS) was used to examine the seriousness of neuropathy in a general and neurological examination. The scores were as follows: 0 to 5 (no neuropathy), 6 to 8 (mild neuropathy), 9 to 11 (moderate neuropathy), and above or equal to 12 (severe neuropathy) [6].

The Nihon Kohden machine was used to perform nerve conduction studies on all individuals, including diabetic peripheral neuropathy with foot ulcerations, in the neurophysiology unit of the neurology department. Conduction velocity, amplitude, and motor distal latency for the ulnar, median, posterior tibial nerves, and common peroneal were

all considered. In addition, the amplitude of the ulnar and the sensory distal latency, median, sural, and superficial peroneal nerves were measured.
Under certain strict conditions, all patients gave 5 ml of venous blood. To evaluate 25-OH vitamin D, the serum and centrifuges were used along with an enzyme-linked immunosorbent assay method known as ELISA. 25-OH vitamin D is said to be the best measuring instrument for vitamin D levels. The results were recorded following these scales: Above and equal to 30 nanograms/dl was recorded as sufficient vitamin D, from 20 to 29 nanograms/dl was recorded as insufficient vitamin D, and below 20 nanograms/dl was recorded as vitamin D deficiency [7].

The institutional review boards approved this research. Each patient's consent was taken before starting the research. SPSS version 22.0 (2013) was used to carry out the analysis of statistics. Categorical variables were demonstrated as n and %. Other quantitative variables were converted into mean standard deviation (SD) and range. The Kolmogorov-Smirnov test was used to test the regularity of the quantitative data. Chi-test was used to examine the percentages of categorical variables. When the number of patients were <5 in the ell, Fisher exact test was used.

Results

There was no difference seen between the demographic characteristics of groups of patients. Results showed that for the occurrence of diabetic peripheral neuropathy, the time span of diabetes is said to be an important factor. With the comparison of other patient groups, patients without diabetic neuropathy had a lower mean of diabetes duration. Most of the individuals were using different drug therapies to manage their diabetes. As many of the individuals used dissimilar drug therapies during the disease course, it became difficult to assess properly the relationship between the occurrence of different types of neuropathy and the therapy used. Group A (with severe pain in diabetes neuropathy) score ranged from 9 to 15, having a mean of 13. Forty percent of them had diabetic foot changes. Group B core ranged from 6 to 9, having a mean of 7.9. Group C results ranged from 6 to 13, having a mean of 9.9. All four groups had a highly statistical difference with respect to the scores of neuropathies.
In terms of the results of nerve conduction experiments performed on individuals, we observed that 100 percent of lower limb nerves are affected, with the peroneal and sural nerves being afflicted.

Table no.1 shows the nerve conduction study of individuals. Group A (with severe pain in diabetic neuropathy) had 71% of patients who had lower vitamin D levels. The level of vitamin D ranged from 5.2-41 nanograms/dl and the mean was 17.6. Group B (with no pain or neuropathy) had 61% of patients who had lower vitamin D levels. The level of vitamin D ranged from 6.4-36.5 nanograms/dl and the mean was 19. Group D (without neuropathy) had only 6% of patients who had vitamin D deficiency. Table no. 2 shows an inverse relationship between neuropathy score and vitamin D level. The lower the vitamin D level, the higher the neuropathy score.
For vitamin D status, the best fitted logistic regression model was used. According to the table, the only independent forecaster of vitamin D status were age and neuropathy score. An LR was used to examine the impact of age, gender, diabetic foot stage, neuropathy score, hemoglobin level, white blood cells, albumin levels, and platelets on the possibility that individuals were vitamin D deficient. As demonstrated in Table 3, those individuals whose neuropathy score was high were 1.5 times probable to be vitamin D deficient. In a logistic regression analysis, old age and an increased score of neuropathies were found to be related to insufficient vitamin D when compared to other covariates which are shown in table no 4.

Table no. 1: Nerve conduction study of individuals

	A		B		C		D	
	no	**%**	**no**	**%**	**no**	**%**	**no**	**%**

Lower limb nerves								
Absent sural SNAP	21	100	21	100	21	100	0	0
Peroneal CMAP								
Normal (N)	13	62	1	5	1	5	21	100
Reduced (R)	7	33	9	43	5	24	0	
Absent	1	5	11	52	15	71	0	
Tibial CMAP								
Normal	16	76	5	24	3	14	21	100
Reduced	5	24	11	52	8	38	0	
Absent	0	0	5	24	10	48	0	
Upper limb nerves								
Median CMAP								
(N)	16	76	13	62	13	62	21	
(R)	5	24	8	38	8	38		
Ulnar CMAP								
(N)	17	81	16	76	13	62	21	
(R)	4	19	5	24	8	38		
Affected median SNAP	2	25	3	22	5	21	2	6

Affected ulnar SNAP	2	4	4	25	2	14	1	100

Table No. 2: Relationship between neuropathy score and vitamin D level

	A		B		C	Control group			χ2/KWt	p-value
	no	%	no	%	No	%	no	%		
Level										
Mean ± SD	17.6		19		20	32.1			63.3	0.000* (HS)
Median (range)	15.3		17		17.9	31.2				
Status										
Deficient	14	67	12	57	13	62	2	1	22.3	0.001* (HS)
Insufficient	4	19	4	19	3	14	7	33		
Sufficient	3	14	5	24	5	24	12	66		

Table No. 3: Neuropathy score with vitamin D levels

Coefficients	Level of vitamin D
R	0.34
p-value	<0.05

Table no. 4: Comparison of **insufficient vitamin D with other covariates**

	B	S.E	Wald	p-value	Exp	CI 95 percent	
						Lower	Upper
Male	− 0.42	0.76	0.52	0.59	0.60	0.17	2.97
Age	1.11	1.04	3.10	1.05	2.15	0.02	2.29
Ulcerated foot	1.42	0.77	1.16	1.73	2.51	1.04	44.04
Infected foot	1.67	0.58	1.47	1.67	2.98	1.08	44.32
Score	0.30	0.11	7.20	0.06	1.31	1.08	1.71
Hemoglobin	0.01	0.49	0.21	0.87	1.03	0.44	2.66
White blood cells	0.08	0.15	0.22	0.87	1.08	0.72	1.44
Platelets	− 0.01	0.01	0.18	0.73	0.99	0.92	1.06
Albumin	0.42	1.28	0.25	0.65	1.69	0.16	17.97

Discussion

Diabetes mellitus is increasing worldwide. Around fifty percent of patients who are affected with diabetes mellitus have diabetic peripheral neuropathy, which is a common problem that is associated with diabetes mellitus. One of the crucial reasons for mortality and morbidity is diabetic peripheral neuropathy. The pathology of diabetic peripheral neuropathy is still not clear [8]. However, some factors such as hypoxia, high blood glucose, low blood flow, pro-inflammatory responses, and hypoxia-induced pro-angiogenesis play a significant part in the pathogenesis. Glial cells, affect nerves, and interleukins are pro-inflammatory cytokines that should be included in diabetic neuropathy pathology. Low levels of vitamin D are a high-risk factor for diabetic peripheral neuropathy because it is related to the existence of inflammation [9].

This research was carried out on 84 individuals who had type 2 diabetic mellitus. This research was conducted to examine the relationship between the development of diabetic neuropathy and serum vitamin D level. This research also evaluates whether there is an association with specific subtypes of diabetic neuropathy. In our research, from the results, we found that a hundred percent of lower limb nerves are affected which is mostly seen in sensory nerves. This shows that mostly long sensory nerves are impacted by diabetic neuropathy [10].

According to Kong et al., the involvement of common peroneal nerves dominates in diabetic peripheral neuropathy [11]. However, according to Kakrani et al., involvement of the tibial nerve is likely to be found in diabetic peripheral neuropathy [12]. Our outcomes are the same as the study of Shillo et al. According to Shillo et al., vitamin D levels

were found lower in those individuals who had diabetic neuropathy, and significantly in those who had severe pain in diabetic neuropathy instead of those without diabetic neuropathy [13].

In a previous study conducted by Usluogullari et al., they assessed vitamin D levels in 55 patients who had T2DM and concluded that the deficiency of vitamin D was found in those diabetic patients who had microvascular issues along with neuropathy. Where the issues were more severe, the level of vitamin D was found to be lower [14].

According to Oraby et al., vitamin D lower levels were observed to be a doubted risk factor for diabetic peripheral neuropathy. They compared individuals with diabetic peripheral neuropathy to healthy controls. The level of vitamin D was low in individuals who were in serious neuropathy [15].

According to Martin et al., if patients with diabetic peripheral neuropathy were provided with vitamin D supplementation along with exercise, there would be a decline seen in the symptoms and complications of diabetes neuropathy [16]. According to Papanas and Ziegler, the deficiency of vitamin D is seen to be a significant risk factor for diabetic neuropathy occurrence [17].

Qu et al., performed a meta-analysis of over 10 studies to examine the part of deficiency of vitamin D in diabetic peripheral neuropathy. It was concluded that although there were low levels of vitamin D seen in individuals with diabetic peripheral neuropathy, it was seen more in Asian and Caucasian races. It was clearly seen that vitamin D deficiency acts as an important part in the occurrence of diabetic neuropathy and it is linked with the high risk of diabetes neuropathy [18].

Greenhagen et al., conducted another trial to examine vitamin D in individuals with diabetic foot problems. In the research of 100 patients, 75% exhibited vitamin D deficiency. However, there was no dissimilarity between individuals with Charcot joints and those without [19]. Zhang et al., analyzed, encompassing more than 13 studies and over 2800 individuals all with T2DM, found an important link between vitamin D and the occurrence of diabetes neuropathy in T2DM individuals [20]. Most prior research found vitamin D insufficiency in diabetic individuals with diabetic neuropathy. Furthermore, more research is needed to know the definite involvement of vitamin D insufficiency in the occurrence of DPN.No prior research could confirm the outcomes of our research.

Conclusion

Our research concludes that the deficiency of vitamin D acts as a significant part in the occurrence of diabetic peripheral neuropathy. This is why we recommend that more research should be conducted to track the betterment of painful neuropathic symptoms in such individuals after vitamin D supplementation. Vitamin D also helps to improve the results of painless neuropathy. Every diabetic patient should have their vitamin D levels checked on a daily basis because lowering the deficiency of vitamin D would result in less occurrence of all subtypes of diabetic peripheral neuropathy.

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Conflict of interest

None

Permission

Permission was taken from the ethical review committee of the Institute

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