Zagazig University Medical Journal
www.zumj.journals.ekb.eg
Volume29, Issue2, March 2023(411-416)

Manuscript ID ZUMJ-2104-2190 (R4)

DOI **10.21608/zumj.2021.71822.2190**

ORIGINAL ARTICLE

Vitamin D Assessment in Diabetic Patients with Peripheral Neuropathy

Nashwa Abo Farrag Sadek [1*], Mohammad Hamdy Assy[1], Ahmed A. Zaghlol[1] and Mohammad Gaber Hamed [1]

[1]Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author:
Nashwa Abo Farrag Sadek Awad Draz, M.B.B.CH, Faculty of Medicine, Zagazig University, Egypt.
E mail:
nashwaf19@gmail.com

Submit Date 2021-04-10
Revise Date 2021-08-07
Accept Date 2021-07-28

ABSTRACT

Background: The diabetes mellitus (DM) prevalence was 525 million in 2019 and type 2 **(**T2DM) around 90% of all cases of diabetes. Diabetic neuropathy (DN) is a micro-vascular complication of DM and considered a major cause of mortality and morbidity in diabetic population. The aim of this study to evaluate the relation between a possible vitamin D level and diabetic neuropathy development.

Methods: A study included 80 patients divided into 4 groups; (A): diabetic patients with painful diabetic neuropathy; (B): diabetic patients with painless diabetic neuropathy; (C): diabetic patients with painless neuropathy and neuropathic ulcer and (D) healthy controls. Serum vitamin D levels was measured in all patients and neurological scoring for neuropathy was assessed.

Results: Patients In group A had neuropathy score from 9 to 15. Patients in group B had Neuropathy score from 7 to14. In group C, patients had neuropathy score from 6 to 9. 60% of group A had deficient vitamin d level. 65% of group B of had deficient vitamin d level. 5% only of the studied healthy control had deficient vitamin D. There was highly statistically significant difference between the four groups regarding vitamin D level and vitamin D status assuming that vitamin D deficiency was below 25 ng/dl.

Conclusions: Vitamin D deficiency is considered as major risk factor for development of diabetic peripheral neuropathy (DNP). Therefore, we recommended to estimate vitamin D level in patients with DPN.

Keywords: Diabetes mellitus ;Vitamin D; Peripheral Neuropathy

INTRODUCTION

The diabetes mellitus (DM) prevalence was 525 million in 2019**.** Diabetes mellitus type 2 **(**T2DM) represented 90% of diabetes disease. During insulin resistance state, insulin is unsuccessful and is initially contradicted by increasing in the insulin production for maintaining the glucose homeostasis, but, the insulin production may decreases which resulting in occurrence of T2DM **(1,2).** Diabetic Peripheral neuropathy (DPN) is a micro-vascular complication of DM and considered a major cause of mortality and morbidity in diabetic population **(3)**. The etiologocal complex of the DPN is not understandable. Nonetheless, the presence of hyperglycemia, blood flow decreasing, hypoxia, and inflammatory responses which may have the responsibility for the pathogenesis **(4).** Deficiency of vitamin D is a supposed as risk factor for DPN due to its relation to the inflammation response and increased blood glucose level **(5)**. Accordingly, vitamin D deficiencies may associated with changes in the incidence of infections **(6)**. Previous studies have assessed the relation of the inflammatory cytokines and deficiencies of vitamin D are thought to have action DPN pathogenesis. The identification of DPN pathogenesis with a modifiable risk factor which may facilitate the presence of a new therapies **(7, 8).** The aim of this study was to evaluate if there is a significant relationship between vitamin D level and development of diabetic neuropathy and to assess if there is association with certain subtypes of diabetic neuropathy.

METHODS

A case control study was carried out in Endocrinology unit and outpatient clinic of Internal Medicine Department, Faculty of Medicine, Zagazig University Hospitals from July to September 2019.

Written informed consent was obtained from all participants. The study followed the principles of the Helsinki Declaration and ethical approval was received from the Institutional Review Board (IRB) of Zagazig University Hospitals.

Inclusion criteria:

Patients have type 2 DM according to WHO criteria with diabetic neuropathies. Neuropathy was defined as self report of peripheral neuropathy symptoms of painful sensation, tingling, numbness or loss of feeling in feet.

Exclusion criteria:

non-diabetic neuropathies: alcoholic, neurological, or other systemic disorders like hepatic failure or renal failure. People on either maintenance or high-dose vitamin D supplementation were also excluded.

A total number of 80 patients were included in the study and were divided into four groups equally. Group A: Diabetic patients who already developed painful diabetic neuropathy (n=20). Group B: Diabetic patients who already developed painless diabetic neuropathy with no ulcers in leg(n=20). Group C: Diabetic patients with painless neuropathy but have neuropathic ulcer(n=20). Control Group: Healthy volunteers underwent clinical and neurological examination(n=20).

Full taking history, examination including neurological examination and neurological scoring for neuropathy were done. All patients had seasonal sunlight exposure and doing activities; measurement was done during summer months.

Serum 25-hydroxyvitamin D (25[OH] D) were measured using ELISA at the four studied groups.

Assessment of peripheral neuropathy was done by neuropathy disability score (NDS) and nerve conduction studies. The NDS was established by bilateral examination of the pin–prick sensation, temperature sensation, vibration test, and Achilles tendon reflex. A score of 0–2 implies no neuropathy, 3–8 is an indicator of mild neuropathy, 8–13 is moderate, and over 14 is consistent with severe neuropathy.

STATISTICAL ANALYSIS

The data were analyzed by computer using the software SPSS 23.0 (IBM, Armonk, NY, USA), Data were represented in tables and graphs, Continuous Quantitative variables e.g. age were expressed as the mean ± SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage). We applied t-test, chi squared test and Kruskal Wallis test for the studied variables. It could considered a significant statistical difference when $P< 0.05$.

RESULTS

The current study showed age of the studied painful diabetic neuropathy group ranged from 45-65 years old with mean 54.30 ± 6.92 years. Half of them were male (50%), also in the painless diabetic neuropathy group their age ranged from 47-86 years old with mean 57.85 ± 9.23 years and 50% of them were male, there was no statistical difference between 4 groups regarding age and sex **(Table 1)**.

The duration of diabetes mellitus among the studied group A ranged from 4 -15 years with mean 8.95 ± 3.42 years, while in the group B (painless diabetic neuropathy) , group C (painless neuropathy with neuropathic ulcer) duration of DM ranged from 3- 17 years and 3 – 14 years respectively. Regarding type of treatment, most of the studied patients were on insulin therapy, there was no statistical difference between groups of diabetic patients regarding type of treatment and duration of disease **(Table 2).**

There was no statistical difference between diabetic patients in presence of hypertension, IHD and COPD, but Charcot joint was found in about 1/3 of painful diabetic neuropathy group with statistically significant difference **(Table 3).**

There was highly statistically significant difference between 4 groups regarding scoring of neuropathy and staging of diabetic foot. The neuropathy score among the studied painful diabetic neuropathy (group A) ranged from 9 – 15 with mean 12.25± 2.14. 55 % of them were had ulcerated foot. in the painless diabetic neuropathy group (group B), neuropathy score ranged from 7-14 with mean 9.7 ± 2.02 and 95% of them had ulcerated foot, **figure (1).** The mean of Vitamin D among the studied painful diabetic neuropathy group (group A) ranged from 5.3 – 36.5 ng/dl with mean 20.12 ± 8.5. 60% of them had deficient vitamin d level deficiency. In the painless diabetic neuropathy group (group B) neuropathy, vitamin D level ranged from 6.5 – 35.5 ng/dl with mean 18.9± 8.4. 65% of them had deficient vitamin d level. 5% only of the studied healthy control had deficient vitamin D level. There was highly statistically significant difference between the four groups regarding vitamin d level and vitamin D status, **figure (2).**

There is significant negative correlation between vitamin D level and score of diabetic neuropathy where the lower vitamin d level the higher diabetic neuropathy score ($r=-0.325$, $p<0.05$) as shown in **Table (4)**.

Table (1): Demographic characteristics of the studied groups

Item	Group A (N=20)		Group B (N=20)		Group C (N=20)		Control group (N=20)		χ2/KWt	P-value
	No.	%	No.	%	No.	%	No.			
Age (years)										
Mean ± SD	54.30 ± 6.92		57.85 ± 9.23		57.55 ± 7.29		54.55 ± 8		2.34	**0.504 (NS)**
Median (Range)	53.5 (45 – 65)		57 (47 – 86)		58.5(45 – 70)		51 (40 – 66)			
Sex										
Male	10	50.0	10	50.0	9	45.0	6	30	2.18	**0.535 (NS)**
Female	**10**	**50.0**	**10**	**50.0**	**11**	**55.0**	**14**	**70**		

χ2 : chi-square test KWt: Kruskal Wallis test. P < 0.05 is significant. NS: Not significant.

Table (2): Treatment and Duration of diabetes among the studied diabetic patients

Item	Group A (N=20)		Group B (N=20)		Group C (N=20)		χ2/ KWT	P-value
	No.	%	No.	%	No.	%		
Type of treatment								
Insulin	18	90.0	17	85.0	16	80.0	0.784	**0.676 (NS)**
OHD	2	10.0	3	15.0	4	20.0		
Duration of DM (years)								
Mean ± SD	8.95 ± 3.42		8.7 ± 3.63		7.6 ± 2.94		1.58	**0.452 (NS)**
Median (Range)	**9(4 – 15)**		**8 (3 – 17)**		**7 (3 – 14)**			

OHD; Oral hypoglycemic drugs χ2: chi-square test , KWt: Kruskal Wallis test. P < 0.05 is significant. NS: Not significant.

Table (3): Co-morbidities among the studied diabetic groups

Item	Group A (N=20)		Group B (N=20)		Group C (N=20)		χ2	P-value
	No.	%	No.	%	No.	%		
Hypertension	9	45.0	7	35.0	10	50.0	0.950	**0.622**
IHD	3	15.0	2	10.0	4	20.0	0.784	**0.676**
COPD	5	25.0	8	42.1	5	25.0	1.42	**0.490**
Charcot joint	**6**	**30.0**	**0**	**0.0**	**0**	**0.0**	**13.33**	**0.001***

IHD; ischemic heart disease, COPD; chronic obstructive pulmonary disease , χ2: chi-square test *P < 0.05 is significant.

Table (4): Correlation between vitamin D level and score of neuropathy

Correlation Coefficient		Vit D level
Score of neuropathy	R	**-.325****
	p-value	**.003**

**. Correlation is significant at the 0.01 level (2-tailed).

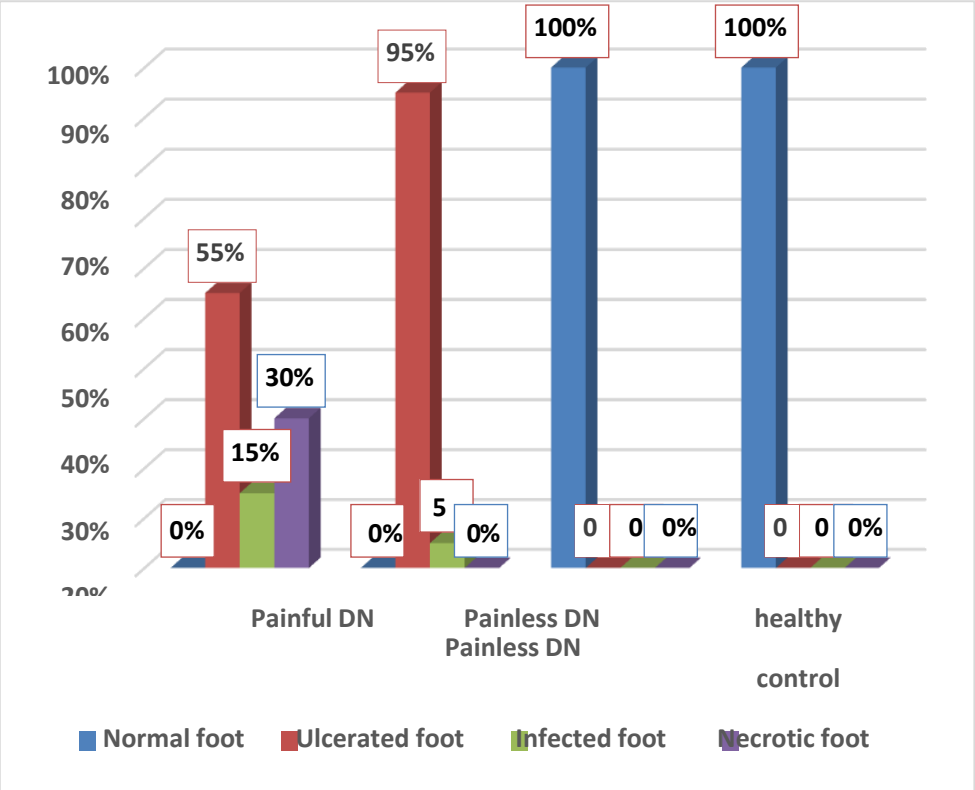

Figure (1): Comparison of stage of diabetic foot among the studied group

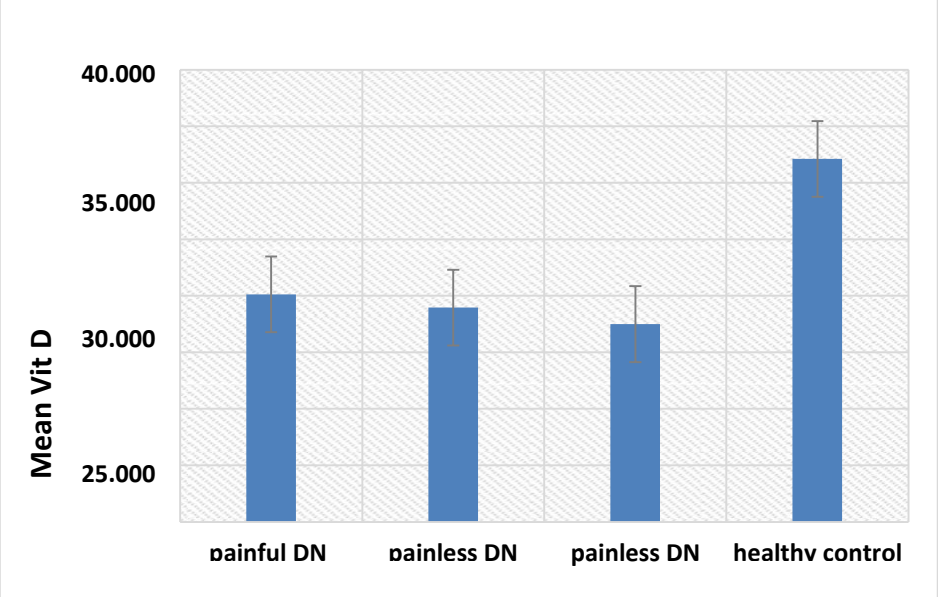

Figure (2): mean vitamin d level among the studied group

DISCUSSION

The present study was to evaluate the relationship between vitamin D deficiency and peripheral neuropathy in T2DM patients. In this study, 80 patients were divided into four equally groups: patients with painful DPN with foot ulcers, patients had painless DPN with no ulcers in foot; patients had painless DPN neuropathy with foot ulcers and control group.

Vitamin D deficiency in diabetic patients is common, and correlated with the severity of diabetic neuropathy. The mechanisms that strengthen the associations of vitamin D and DPN are not implicited. Pain sensitivity associated to vitamin D levels which mediated by dorsal root ganglia and small nerve fibers **(9,10).**

In our study, patients in group A had neuropathy score from 9 to 15. Patients in group B had Neuropathy score from 7 to14. In group C, patients had neuropathy score from 6 to 9. in group D only 5% from them had vitamin D deficiency.

This study concur **Ghadiri-Anari et al.(2)** who enrolled 60 T2DM subjects (30 to 65 years old) with diabetic neuropathy. Evaluation of diabetic neuropathy was performed by using Michigan Neuropathy Screening Instrument (MNSI) before and after trial including (Symptom scores, Reflex scores, Sensory test scores). They found supplementation of vitamin D once weekly for 12 weeks was associated with improvement in the serum level of vitamin D and significant decrease in the symptoms and sign of diabetic neuropathy.

The mean of Vitamin D among the studied painful diabetic neuropathy group (A) was 20.12 ng/dl. In the painless diabetic neuropathy group (B), vitamin D mean was 18.9 ng/dl.. In group C, The level of vitamin D was ranged from 5.3 to 50.5 ng/dl. About 5% only of the studied healthy control had deficient vitamin D. There was highly statistically significant difference between the four groups regarding vitamin D level and vitamin D status assuming that vitamin D deficiency was below 25 ng/dl.

Our study was agree with **Bilir et al. (3)** who compared patients with DPN and diabetic patients to healthy controls. They found that vitamin D deficiency suspected for DPN as the results of this study in diabetic patients compared to control group. For the meantime, vitamin D levels of the DPN group were inferior to patients with non-neuropathic diabetes. However, in our study, we determined the level of decreased seum vit. D in each group and found a significance difference in between.

This was in agreement with study of **Usluogullari et al. (5)** who evaluated vitamin D level in 557 patients with diabetes. The 25-OH vitamin D levels in patients with T2DM and subsequence, micro vascular complications were diagnosed. Study revealed that vitamin D deficiency in the diabetic patients associated neuropathy and micro-vascular complications.Strengths of our study was evaluating the possible relation between a vitamin D deficiency and groups of patients with diabetic neuropathy in different stages of signs (i.e presense of pain and ulcer) and assed the level of vitamin D in the different groups.

Several studies revealed that oral and topical vitamin D supplementation leads to improvement of the neuropathy symptoms **(11).** Another study evaluated the efficacy and safety of vitamin D2 supplementation in type 2 diabetic with DPN, they found improvement in clinical symptoms and nerve conduction velocity **(12)**.

Further studies are needed to confirm the degree of response for treated different signs of diabetic neuropathy cases with vitamin D supplementation with accurate and safe administration for diabetic patients.

CONCLUSIONS

Vitamin D deficiency may be considered a risk factor for development of diabetic peripheral neuropathy (DNP). Therefore, we recommended to estimate vitamin D level in patients with DPN.

Future studies are needed to evaluate the definitive role of vitamin D deficiency in development of DPN and nerve conduction studies.

Declaration of interest: The authors declare no conflict of interest.

Funding: The authors have no funding to report.

REFERENCES

1. Deshpande A, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Phys Ther , 2008 1;88(11):1254-64.
2. Ghadiri-Anari A, Mozafari Z, Gholami S. Dose vitamin D supplementations improve peripheral diabetic neuropathy? A before-after clinical trial. Diabetes Metab Syndr. 2019;13(1):890-893.
3. Bilir B, Tulubas F, Bilir B. The association of vitamin D with inflammatory cytokines in diabetic peripheral neuropathy. J Phys Ther Sci. 2016;28(7):2159-63.
4. Qu G, Wang L, Tang X, Wu W, Sun H. The association between vitamin D level and diabetic peripheral neuropathy in patients with type 2 diabetes mellitus: An update systematic review and meta-analysis. J Clin Transl Endocrinol. 2017;9:25-31.
5. Usluogullari C, Balkan F, Caner S. The relationship between microvascular complications and vitamin D deficiency in type 2 diabetes mellitus. BMC Endocr Disord. 2015;15:33. Published 2015 Jun 25.
6. Qu G, Wang L, Tang X, Wu W, Sun Y. The association between vitamin D level and diabetic peripheral neuropathy in patients with type 2 diabetes mellitus: An update systematic review and meta-analysis. J Clin Transl Endocrinol. 2017;9:25-31.

7. Zhang B, Zhao W, Tu J, Wang X., Hao Y., Wang H., et al. The relationship between serum 25-hydroxyvitamin D concentration and type 2 diabetic peripheral neuropathy: A systematic review and a meta-analysis. Medicine (Baltimore). 2019;98(48): 18118.
8. Alamdari A, Mozafari R, Tafakhori A, Faghihi-Kashani S, Hafezi-Nejad N, Sheikhbahaei S, et al. An inverse association between serum vitamin D levels with the presence and severity of impaired nerve conduction velocity and largefiber peripheral neuropathy in diabetic subjects. Neurol Sci 2015;36(7):1121e6.
9. Shehab D, Al-Jarallah K, Mojiminiyi O, Al Mohamedy H, Abdella NA. Does Vitamin D deficiency play a role in peripheral neuropathy in Type 2 diabetes? Diabet Med 2012;29(1):43e9.
10. Bajaj S, Singh RP, Dwivedi NC, Singh K, Gupta A, Mathur M. Vitamin D levels and microvascular complications in type 2 diabetes. Ind J Endocrinol Metabol 2014;18(4):537.
11. Abdelsadek E, El Saghier O, Raheem A.. Serum 25 (OH) vitamin D level and its relation to diabetic peripheral neuropathy in Egyptian patients with type 2 diabetes mellitus. Egy J of neuro psy neurosurg,2018; 54(1), 1-8.
12. Yueyue Z, Xiaoxia S, Dexue L, Ruige L. Efficacy and safety of vitamin D2 supplementation on diabetic peripheral neuropathy: a multicentre, randomised, double-blind trial. Lancet Diabet Endocrinol; 2016;4:S29.

To Cite:
Sadek, N., Assy, M., Zaghlol, A., Hamed, M., Vitamin D Assessment in Diabetic Patients with Peripheral Neuropathy. *Zagazig University Medical Journal*, 2023; (411-416): -.doi: 10.21608/zumj.2021.71822.2190.