



Original Research Article

Relationship of Serum Vitamin D levels with Nerve Conduction Velocity in patients of Diabetic Neuropathy

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ABSTRACT

Introduction: Although vitamin D insufficiency is very prevalent in Type-2 diabetes mellitus, there are no studies to prove its role or association in diabetic peripheral neuropathy.

Aims and Objectives: We intend to highlight the relationship of Serum Vitamin D levels with Nerve Conduction Velocity in patients of Diabetic Peripheral Neuropathy.

Material and Methods: 52 patients of diabetic neuropathy were assessed for sensory and motor nerve conduction velocity along with serum Vitamin D levels estimation and the results were statistically analyzed.

Results: Tingling was the most common symptom, seen in 31.1% cases. The numbers of nerve involvement increased with the duration of diabetes mellitus. Majority of the patients showed decrease in SNCV and MNCV in more than three nerves, 17(32.69%) and 15(28.84%) cases. 14(87.5%) vitamin D deficient patients had HbA1c levels >11.5. Vitamin D deficiency was more pronounced than insufficiency as the HbA1c levels got increased. The vitamin D deficiency increased in proportion to the duration of disease, with maximum number of vitamin D deficient patients in the disease duration of 11-15 years followed by vitamin D deficient patients with duration of disease >15 years. 36(69.2%) of the diabetic patients were deficient in vitamin D, followed by vitamin D insufficiency in 14(26.9%) (p value < 0.001). Among the vitamin D deficient patients, females were in excess of males, (52.8%), (p value = 0.314)

Conclusions: Nerve conduction velocities and vitamin D deficiency might be independently associated with diabetic peripheral neuropathy, so these investigative parameters could be used as an independent marker to assess the severity of the neuropathy.

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1. Introduction

Diabetes mellitus is known as a group of common metabolic disorders, mainly a condition that has presence of a chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism associated absolute or relative insulin deficiencies in their secretions and action.¹

Diabetes is one of the most important leading cause of blindness (retinopathy), end stage renal disease and a variety of debilitating neuropathies.² Diabetic neuropathy is the most common complication diabetes mellitus and also the major leading cause of morbidity and mortality in diabetic patients.³ There have been recent speculations that circulating 25-hydroxyvitamin D (25(OH)-D) could be involved in the Diabetic neuropathy development and its progression.^{4,5}

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A very important role is played by vitamin D in metabolic disease, like diabetes mellitus. It appears that lower level of vitamin D is mainly related to neuropathy development and predisposes to many other neurodegenerative disorders, suggesting that treatment with vitamin D can lead to correction of these predisposing metabolic disturbances in the body.⁶ We intend to highlight the relationship of serum Vitamin D levels with Nerve Conduction Velocity (NCV) in patients of Diabetic Neuropathy in the present study.

2. Materials and Methods

This prospective study was conducted on 52 patients with Diabetic Neuropathy, after approval from ethical committee of the college and taking written informed consent from the patients. The baseline characteristics were compared between age and sex matched type 2 diabetic patients having peripheral neuropathy with healthy controls.

A detailed history and thorough physical examination was carried out on every case in the study as per a pre-designed proforma. Selected cases of Type 2 Diabetes Mellitus patients were assessed for diabetic peripheral neuropathy by both sensory and motor nerve conduction velocity (Apparatus: NeuroStim4-NS4 EMG/NCV/EP SYSTEM, Medicaid, India). Selected patients were assessed with neuropathy symptom score (NSS) with symptoms of paresthesias like burning/numbness/tingling/cramping/aching and clinical examination for neuropathy disability score (NDS). Blood samples were collected in EDTA vials for estimation of HbA1C, Sodium Fluoride vials for plasma glucose, in plain vial for serum Vitamin D by the "LIAISON DiaSorin 25-OH Vitamin D assay". Blood for fasting and post prandial glucose estimation was collected on the same day. All the data was statistically analyzed using SPSS software version (20.0). Statistical analysis was performed by Chi square tests and ANOVA according to the variables and the comparisons needed. p-value of 0.05 or less was considered to be statistically significant.

3. Observations

Our study included 52 provisionally diagnosed patients of peripheral neuropathy comprising of 27 males and 25 females, who met the inclusion/exclusion criteria and had given valid written consent. A group of 12 normal individuals without diabetes served as control in our study.

The most common symptom was tingling in 20(31.3%) cases, followed by tingling and numbness in 14(21.9%) burning sensation and tingling in 6(9.4%) and weakness of limbs and cramping in 5(7.8%) patients.

Majority of the patients showed decrease in SNCV in more than three nerves; 17(32.69%), followed by three nerves in 13(25.0%) patients (Table 1). Majority of the

patients showed decrease in MNCV in more than 3 three nerves; 15(28.84%), followed by three nerve involvement in 13(25.0%) patients (Table 2).

Thirty six (69.2%) of the diabetic patients were deficient in vitamin D, followed by vitamin D insufficiency in 14(26.9%) (p value<0.001). Among the vitamin D deficient patients, females were in excess of males, (52.8%), (p value=0.314) (Table 3). The vitamin D deficiency increased in proportion to the duration of disease, with maximum number of vitamin D deficient patients in the disease duration of 11-15 years followed by vitamin D deficient patients with duration of disease>15 years (Table 4).

Majority of the vitamin D deficient patients had higher levels of HbA1c, with 14(87.5%) patients having HbA1c levels >11.5. Vitamin D deficiency was more pronounced than insufficiency as the HbA1c levels got increased (Tables 5 and 6).

Table 1: Sensory nerve conduction velocity (SNCV) findings in patients of diabetes.

Observations	Number of patients	Percentage
No impact-normal SNCV	03	05.8
Decrease in SNCV of one nerve	10	19.2
Decrease in SNCV of two nerves	09	17.3
Decrease in SNCV of three nerves	13	25.0
Decrease in SNCV of > 3 nerves	17	32.7
Total	52	100.0

Table 2: Motor nerve conduction velocity (MNCV) finding in diabetic patients

Observations	Number of patients	Percentage
No impact-normal MNCV	04	7.7
Decrease in MNCV of one nerve	08	15.4
Decrease in MNCV of two nerves	12	23.1
Decrease in MNCV of three nerves	13	25.0
Decrease in MNCV of ≥ 3 nerves	15	28.8
Total	52	100.0

4. Discussions

The most common symptom was tingling in 20(31.3%) cases, followed by tingling and numbness in 14(21.9%) burning sensation and tingling in 6(9.4%) and weakness of limbs and cramping in 5(7.8%) patients. Similar symptoms were shown in the study by Pop-Busui et al.²

Table 3: Vitamin D levels in the diabetic cases.

Vitamin D levels	Male		Female		Total		Chi square value=32.842 p<0.001
	No.	%	No.	%	No.	%	
Deficiency	17	47.2	19	52.8	36	69.2	
Insufficiency	10	71.5	04	28.5	14	26.9	
Sufficiency	02	100.0	00	00	02	03.8	
Total	29	55.8	23	44.2	52	100.0	

Table 4: Vitamin D levels according to duration

Duration of diabetes (years)	Number of patients with vitamin D levels		
	Deficiency	Insufficiency	Sufficiency
0-5	02	02	00
6-10	09	04	00
11-15	14	02	02
>15	12	05	00
Total	37	13	02

Table 5: Relationship of Vitamin D levels with HbA1c levels.

HbA1c levels (%)	Number of patients with different vitamin D levels							
	Deficiency		Insufficiency		Sufficiency		Total	
	No.	%	No.	%	No.	%	No.	%
6.6-7.5	00.0	00	03	100	00.0	00.0	03	05.7
7.6-8.5	05	62.5	03	37.5	00.0	00.0	08	15.4
8.6-9.5	09	69.3	03	23.0	01	07.7	13	25.0
9.6-10.5	04	57.2	02	28.6	01	14.2	07	13.5
10.6-11.5	05	83.4	01	16.6	00.0	00.0	06	11.5
>11.5	13	86.7	02	13.3	00.0	00.0	15	28.9
Total	36	69.2	14	26.9	02	03.8	52	100.0

Table 6: Comparison between baseline characteristics of controls(n=12) v/s Type 2 Diabetic subjects(n=52)

Variable	Controls (n=12)		Diabetic subjects (n=52)	P value
	Male	Female		
Number				0.689
Age (years)			7	27
Duration of T2DM(years)			5	25
Fasting plasma Glucose (mg/dl)			55.17±13.11	56.42± 11.58
Post prandial glucose (mg/dl)			0	12.90± 5.02
HbA1c (%)			93±10.67	167.02±25.87
Vitamin D (ng/dl)			119.75±15.43	223.18±50.72
Right sided SNCV(m/s) of			5.54±0.36	10.50±2.21
Left sided SNCV(m/s) of			42.49±6.99	17.22±6.82
Right sided MNCV(m/s) of			49.6±1.2	42.1±4.2
Left sided MNCV(m/s) of			52.7±1	46.3±6.5
			51.5±1	48.4±4.8
			49.8±1	41.8±4.2
			52.3±1	47.6±5.7
			52.2±1.5	48.3±4.8
			48.9±2	42.5±3.4
			48.8±1.5	42.7±3.5
			55.9±1	49.2±7.8
			48.2±1.8	42.7±3.3
			48.5±1.3	44.1±1.6
			55.2±1	51.8±2.9

The age range of type 2 diabetic patients with neuropathy was between 30-77 years old with average of 56.4 ± 11.6 years. Similar results were shown by study done by Popescu et al who reported a median age of the diabetic patients as 62 years.³ In our study, we found the prevalence of diabetic peripheral neuropathy to be 32.2%. Tesfaye et al, Pradeepa et al and Gill et al have stated a prevalence of 28.0%, 26.1% and 29.4% respectively.⁴⁻⁶

With increasing age of diabetic patients, the incidence of diabetic complications of peripheral neuropathy increased. In our study the number of patients of diabetic peripheral neuropathy increased with age from 11.5% in the age group of 31-40 years old to 38.5% in the age group of >60 years old. Our finding was consistent with Morkrid et al who reported the prevalence of diabetic neuropathy as 11.1% in the 23-40 years old age-group and 32.3% between 60-80 years.⁷ Similar results have also been reported in the study by Zoungas et al.⁸

Twenty seven (51.9%) cases were males and 25(48.1%) were females with a male to female ratio of 1:08 in our study. So, the gender-wise distribution of cases did not show any significant difference.

We found that the duration of diabetes mellitus played an important role on the development of diabetic neuropathy. Majority of the diabetic patients with neuropathy had duration of the disease of more than 10 years, 34(65.4%) patients followed by 14(26.9%) patients with 6-10 years of duration of diabetes. Similar results have been reported by Deshpande et al.⁹

The glycemic status of the type 2 diabetic mellitus patients with neuropathy was higher in most of the patients, 28.9% patients had HbA1c level >11.5% with the major gender being females, comprising 53.4% cases. Also, as the duration of the disease increased, the HbA1c levels got increased in our patients which subsequently lead to diabetic neuropathy. So, a long duration of diabetes and poor glycemic control leads to increased occurrence of diabetic neuropathy. Oguejiofor et al found a lower prevalence of polyneuropathy with duration of diabetes mellitus <5 years and high prevalence with a duration of diabetes mellitus >15 years.¹⁰ Similar findings were also shown by Nisaret al in their study.¹¹

For assessing diabetic peripheral neuropathy, sensory and motor nerve conduction velocities of peripheral nerves were done, both in upper and lower limbs. It is considered as a gold standard for diagnosis of neuropathy.¹² In our study, we assessed nerve conduction velocities of 6 pairs of peripheral nerves comprising of 3 pairs of sensory nerves and 3 pairs of motor nerves. We found statistically significant decrease in nerve conduction velocities of all the nerves assessed in the cases of neuropathy as compared to the controls (p value < 0.05). A study by Tehrani et al showed similar results.¹³

We found that the numbers of peripheral nerve involvement was more as the duration of diabetes mellitus increased from 7.7% in 1-5 years to 32.7% in 11-15 years duration. The association between the duration of diabetes mellitus and neuropathy was also evident in several research studies by Nisar et al and Maser et al on the epidemiology of diabetic complications.^{11,14}

There was early involvement of sensory nerves as compared to motor nerves in patients of diabetic neuropathy. This finding is consistent with the reports of Halar et al and Nascimento et al.^{15,16} We also found that there was involvement of only the sural nerve in many patients, which was also the earliest and most common nerve to be affected. Similar findings have been reported in studies by Riihimaa et al and Karsidag et al.^{17,18}

An association between vitamin D deficiency and prevalence of type 2 diabetes mellitus with neuropathy was seen; 69.3% of our patients were deficient in vitamin D. Similar results were shown by Qu et al.¹⁹ Also, we found that the level of vitamin D was lower in patients with longer duration of type 2 diabetes mellitus. Penckofer et al also suggested that there is decrease in vitamin D status as the duration of type 2 diabetes mellitus increases.²⁰ The vitamin D deficiency was more in females, constituting 19(52.8%) cases. Similar results have been shown in a study by Bayani et al.²¹

We found that most of the patients who were deficient in vitamin D had higher levels of HbA1c levels. Among 36(69.3%) patients who were deficient in vitamin D (i.e vitamin D <50 nmol/l), 13(36.2%) had HbA1c levels >11.5%. This showed a negatively significant coefficient of correlation between vitamin D levels and HbA1c levels which means vitamin D levels showed independent inverse association with HbA1c levels. Similar results have been shown by Buhary et al who reported 73.1% of patients with vitamin D levels < 50 nmol/l with mean HbA1c value of $10.55 \pm 2.58\%$.²² Dalgard et al, Ghavamzadeh et al and Zhang et al have demonstrated that patients of type 2 diabetes mellitus with hypovitaminosis D are more likely to have raised HbA1c levels.²³⁻²⁵

5. Conclusions

As the detection of the various dormant signs of diabetic neuropathy at the earliest could minimize the damaging effects and improve the quality of life; it is recommended that nerve conduction velocity test should be performed on all diabetic patients routinely. Also screening of such patients is very essential with monitoring of HbA1c and serum vitamin D. Vitamin D deficiency might be independently associated with peripheral neuropathy in type 2 diabetes mellitus, so investigative parameters like Vitamin D could be used as an independent marker to assess the severity of diabetic neuropathy.

6. Source of Funding

None.

7. Conflict of Interest

None.

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