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Original Research Article

Electrophysiological estimation of subclinical neuropathy and its types in diabetes mellitus patients

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ABSTRACT

Overview: Diabetes mellitus is the leading cause for peripheral neuropathy in India. It is a devastating complication which leads to amputation of limbs affecting the physical and social quality of life. Subclinical peripheral neuropathy is one which doesn't have any symptoms or signs, but positive electrophysiological findings.

Aims: 1): To estimate the prevalence of subclinical peripheral neuropathy and its types among the diabetes mellitus patients. 2): To determine the various risk factors influencing them.

Materials and Methods: 51 patients with diabetes mellitus without symptoms and signs of peripheral neuropathy were selected based on inclusion criteria and after assessing the screening scores. Necessary blood investigations was done and nerve conduction test was carried out in both upper and lower limbs for motor and sensory study.

Results: 22(43%) out of the 51 diabetic patients had subclinical peripheral neuropathy. Lower limb(29.5%) predominates than upper limb, sensory(23.5%) more common than motor neuropathy. Axonal neuropathy was the predominant (29%). Statistical significance was observed between the duration of diabetes mellitus, high triglyceride levels, high blood sugar profile and high HbA1C values with the presence of subclinical peripheral neuropathy.

Conclusion: Nerve conduction study is the best for diagnosing subclinical neuropathy in diabetes mellitus patients. By early diagnosis and control of diabetes we can prevent dreadful complications.

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1. Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by elevated levels of blood glucose. The prevalence of diabetes in worldwide has been increasing dramatically over the past two decades and is becoming a major global health problem.

Diabetes related complications affect many organs and can be classified as vascular and non-vascular, which contributes to morbidity and mortality. One of the common

and troublesome complications of diabetes mellitus is peripheral neuropathy. It is one of the microvascular complications of diabetes mellitus. It predominates among the other complications due to delay in diagnosis and is often neglected by the patients. Diabetic neuropathy occurs in 50% of individuals with long standing type1 and type2 diabetes mellitus.¹ It may manifest as polyneuropathy, mononeuropathy, autonomic neuropathy. Additional risk factors are body mass index, smoking, elevated triglyceride, hypertension.¹ The most common neuropathy is distal symmetrical polyneuropathy. It most frequently presents with distal sensory loss and pain, but up to 50% can be

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asymptomatic.² These asymptomatic patients will present at later stage with symptoms and signs of peripheral neuropathy. Subclinical neuropathy is one which has no clinical symptoms and signs of neuropathy but a positive electrodiagnostic test.²

Diabetic neuropathy is responsible for 50-75% of non-traumatic amputations.³ It predisposes patients to severe functional limitations and are associated with substantial health care costs, loss of work and reduced quality of life. So it is better to identify such patients at an early stage and control their blood sugar adequately to prevent these adverse outcomes. Hence this study is done to find the prevalence, risk factors and types of subclinical peripheral neuropathy among diabetics in South Indian population in a tertiary care hospital.

2. Objectives

1. To estimate the prevalence of subclinical peripheral neuropathy and its types among diabetes patients.
2. To determine the various risk factors influencing them.

3. Materials and Methods

This study was done at Sri Manakula Vinayagar Medical College and Hospital, Puducherry, under the department of General Medicine in collaboration with department of Neurology during the year 2018-20 after getting institution ethics committee approval. This is a hospital based analytical cross sectional study. Sample size of this study was 51.

3.1. Inclusion criteria

1. Type 1 diabetes patients with age more than 18 years and duration of illness 5 years or more, who do not have neuropathy clinically.
2. Type 2 diabetes patients with age more than 18 years who do not have neuropathy clinically.

3.2. Exclusion criteria

1. Patients having symptoms and signs of peripheral neuropathy.
2. Drugs/Toxins causing neuropathy, alcoholism
3. Chronic kidney disease, vitamin deficiency, connective tissue disease, hypothyroidism.
4. Leprosy, HIV.

Diabetes patients attending general medicine OPD were screened for the inclusion criteria and selected randomly. Appropriate questionnaire was used to collect details of the patients and detailed clinical and neurological examination was done and appropriate screening for neuropathy was done with the help of United Kingdom screening test and Michigan neuropathy screening test to exclude patients who are having clinical symptoms and signs of neuropathy and

include only those who do not have any signs and symptoms for neuropathy.⁴ Blood was collected after getting consent for fasting, postprandial blood sugar, HbA1C, complete blood count, renal function test and fasting lipid profile.

Assessment of nerve conduction study for both upper and lower limbs was done with by nerve conduction instrument with a trained technician and report was interpreted by the Neurologist. The instrument tests nerve conduction by stimulating the median, ulnar, peroneal, tibial nerve for motor function and median, ulnar, sural, superficial peroneal nerve for sensory function with current from 5ma to 100ma.

The data obtained from the proforma was entered into Microsoft excel and analyzed using Statistical Package for Social Sciences version 16. A p value of less than 0.05 was considered statistically significant.

4. Results

4.1. General variables

From Table 1 majority of the participants were males (52.9%) belonging to the age group of 41-60 years.

From Table 2 many of these patients had history of diabetes mellitus for around 6-10 years (76.5%). More than one-third patients had hypertension (35.3%) as a co-morbidity and 78.4% of these diabetic patients were on oral hypoglycaemic drugs.

From Table 3 about 10% and 33% of the patients had high cholesterol and triglyceride levels respectively. Among these diabetics, nearly 50% and 70% of them had higher fasting and postprandial blood glucose levels respectively. On assessing for HbA1C, more than 90% patients had higher HbA1C levels.

Table 4 shows the screening process of the patients for neuropathy with two scales- United Kingdom score and Michigan Neuropathy score. Since all the patients had scores of <2 in both the scales, they had no neuropathy and were eligible for the current study.

4.2. Subclinical neuropathy (SCN)

Figure 1 shows the distribution of subclinical neuropathy among the upper and low limbs. Among the 51 patients, 7 (13.7%) had atleast one of the upper limb nerves affected while 15 (29.4%) had one of the lower limb nerves affected.

The above Figure 1 shows the affected nerves with neuropathy in the upper limb. Both (right and left) median motor nerves were the most involved followed by both median sensory nerves and left ulnar sensory nerve.

The above Figure 3 shows the affected nerves with neuropathy in the lower limb. Both (right and left) superficial peroneal nerves were the most involved followed by both sural nerves.

From Table 6, 23.5% showed subclinical neuropathy in the sensory nerves, 7.8% showed in motor nerves while 11.8% showed subclinical neuropathy in both sensory and

motor nerves.

From Table 7, 29.4% had only axonal neuropathy, 3.9% showed demyelinating neuropathy while 9.8% showed both axonal and demyelinating neuropathy.

Fig. 1: Distribution of subclinical neuropathy among the upper and lower limb never (n=51)

Fig. 2: Distribution of the nerves involved in the upper limb among the patients (n=51)

Fig. 3: Distribution of the nerves involved in the lower limb among the patients (n=51)

Fig. 4: Distribution of triglyceride levels with subclinical neuropathy among the patients (n=51)

4.3. Factors associated with SCN among the subjects

From Table 9, higher duration of diabetes mellitus (DM>10 years) was significantly associated ($p=0.011$) with the presence of subclinical neuropathy among these diabetic patients.

From Table 10, only high triglyceride levels were significantly associated ($p=0.001$) with the presence of subclinical neuropathy among these diabetic patients while all other lipid profile parameters turned out to be statistically non-significant.

From Table 11, all the three blood glucose levels were significantly associated ($p<0.05$) with the presence of subclinical neuropathy. Higher fasting glucose levels ($p=0.002$), higher postprandial glucose levels ($p=0.009$) and higher HbA1C levels ($p=0.016$) were significantly associated with the presence of subclinical neuropathy.

5. Discussion

5.1. Patients characteristics and DM

The sample size of our study was 51. The sample size of this study was nearly equal to the studies conducted by Salem,⁵ Jong,⁶ Meena⁷ and was greater as compared to the studies conducted by Maruti,⁸ Sherman,⁹ Patel,¹⁰ Zhijun,¹¹ Devdutt.¹² In our study all patients were type 2 diabetic and 60% of patients were in the age group of 41 to 60 years and majority of diabetic patients were male (53%). The average duration of diabetes mellitus in this study subjects was around 6 to 10 years with a mean of 8 years. About 78% of the diabetic patients in this study group were on oral hypoglycaemic agents. About 35% of patients had associated hypertension as co-morbidity.

In our study it was observed that majority of patients were taking oral hypoglycaemic agent for diabetes (78.4%). Due to less number of patients taking insulin in our study there might be an increased risk for these patients taking oral agents for getting neuropathy when their blood sugar becomes uncontrolled, as we all knew that insulin has added protective role in diabetic neuropathy.¹³

Table 1: Baseline socio-demographic characteristics of the patients (n=51)

Variable	Categories	Number	Percentage
Age	21-40 years	2	3.9
	41-60 years	31	60.8
	61-80 years	18	35.3
Gender	Male	27	52.9
	Female	24	47.1

Table 2: Morbidity profile of the patients (n=51)

Variable	Categories	Number	Percentage
Duration of Diabetes mellitus	≤5 years	6	11.8
	6-10 years	39	76.5
	> 10 years	6	11.8
Hypertension status	Absent	33	64.7
	Present	18	35.3
Type of Anti-diabetic drugs	Oral Hypoglycaemic agents	40	78.4
	Insulin	4	7.8
	Both	7	13.7

Table 3: Biochemical profile of the patients (n=51)

Variable	Categories	Number	Percentage
Hemoglobin	Normal	18	35.3
	Anaemia	33	64.7
Total cholesterol	Normal	46	90.2
	Hypercholesterolaemia	5	9.8
HDL cholesterol	Low	16	31.4
	Normal	35	68.6
LDL cholesterol	Low	6	11.8
	Normal	44	86.3
Triglyceride	High	1	2.0
	Normal	34	66.7
	High triglyceride levels	17	33.3
Fasting Glucose level	Normal	26	51.0
	High	25	49.0
Post-prandial Glucose level	Normal	16	31.4
	High	35	68.6
HbA1C	<6.5	4	7.8
	6.5-9	33	64.7
	>9	14	27.5

Table 4: Screening profile of the patients for neuropathy (n=51)

Variable	Score	Number	Percentage
United Kingdom Score	0	48	94.1
	1	3	5.9
Michigan Neuropathy Score	0	50	98.0
	1	1	2.0

Table 5: Prevalence of subclinical neuropathy among the patients (n=51)

Variable	Categories	Number	Percentage
Subclinical neuropathy	Present	22	43.1
	Absent	29	56.9

Table 6: Distribution of motor and sensory neuropathy among the patients (n=22)

Neuropathy	Number	Percentage
Pure Motor	4	7.8%
Pure Sensory	12	23.5%
Mixed (both sensory and motor)	6	11.8%

Table 7: Distribution of axonal and demyelinating neuropathy among the patients (n=22)

Neuropathy	Number	Percentage
Pure Axonal	15	29.4%
Pure Demyelinating	2	3.9%
Mixed (both axonal and demyelinating)	5	9.8%

Table 8: Association of demographic factors with the subclinical neuropathy among the patients (n=51)

		Subclinical neuropathy n(%)		Chi-square (p value)
		Present	Absent	
Age category	21-40 years	1 (4.5%)	1 (3.4%)	0.223 (0.895)
	41-60 years	14 (63.6%)	17 (58.6%)	
	61-80 years	7 (31.8%)	11 (37.9%)	
Gender	Male	13 (59.1%)	14 (48.3%)	0.587 (0.443)
	Female	9 (40.9%)	15 (51.7%)	

Table 9: Association of morbidity profile with the subclinical neuropathy among the patients (n=51)

		Subclinical neuropathy n(%)		Chi-square (p value)
		Present	Absent	
Duration of Diabetes mellitus	≤5 years	2 (9.1%)	4 (13.8%)	8.978 (0.011)
	5-10 years	14 (63.6%)	25 (86.2%)	
	> 10 years	6 (27.3%)	0	
Hypertension status	Absent	16 (72.7%)	17 (58.6%)	1.09 (0.296)
	Present	6 (27.3%)	12 (41.4%)	
Type of Anti-diabetic drugs	Oral Hypoglycaemic agents	20 (90.9%)	20 (69.0%)	3.68 (0.159)
	Insulin	1 (4.5%)	3 (10.3%)	
	Both	1 (4.5%)	6 (20.7%)	

Table 10: Association of lipid profile with the subclinical neuropathy among the patients (n=51)

		Subclinical neuropathy n(%)		Chi-square (p value)
		Present	Absent	
Total Cholesterol levels	Normal	19 (86.4%)	27 (93.1%)	0.643 (0.423)
	Hypercholesterolaemia	3 (13.6%)	2 (6.9%)	
LDL cholesterol levels	Low	1 (4.5%)	5 (17.2%)	3.128 (0.079)
	Normal/ high	21 (95.5%)	24 (82.8%)	
Triglyceride levels	Normal	9 (40.9%)	25 (86.2%)	11.551 (0.001)
	High	13 (59.1%)	4 (13.8%)	

Table 11: Association of blood glucose profile with subclinical neuropathy among the patients (n=51)

		Subclinical neuropathy n(%)		Chi-square (p value)
		Present	Absent	
Fasting Blood Glucose levels	Normal	6 (27.3%)	20 (69%)	8.702 (0.002)
	High	16 (72.7%)	9 (31%)	
Post prandial blood glucose levels	Normal	3 (13.6%)	13 (44.8%)	5.653 (0.009)
	High	19 (86.4%)	16 (55.2%)	
HbA1C levels (%)	<6.5	0	4 (13.8%)	8.220 (0.016)
	6.5-9	12 (54.5%)	21 (72.4%)	
	>9	10 (45.5%)	4 (13.8%)	

5.2. Biochemical variables and DM

Majority of our study patients (64.7%) had anaemia which indirectly depicts the chronicity of the diabetes and the mean duration of diabetes in our study was also 8 years. Triglyceride was high in 33.3% of patients. High triglyceride is also a risk factor and a prognostic factor for diabetic neuropathy.¹⁴ So these patients were prone to develop diabetic neuropathy. In our study about half of the patients (49%) had a fasting blood sugar value of more than 126mg/dl with a mean value of 152mg/dl. Post prandial blood sugar was high in nearly more than half of the patients i.e. 68.6% with a mean value of 240mg/dl. HbA1C was high in almost 92% of patients with a mean value of 8.4%. This high value makes these patients at risk for developing peripheral neuropathy and other complications of diabetes mellitus. Such a high HbA1C mean might be explained by the oral hypoglycaemic agent which was taken by 78% of the study patients contributing to the poor control of blood sugar in a longer run and also poor compliance to treatment.

5.3. Subclinical neuropathy and DM

Out of 51 patients enrolled in our study, 22 patients (43%) were diagnosed to have subclinical neuropathy by nerve conduction study while the remaining 29 patients had normal nerve conduction. This subclinical neuropathy was diagnosed based on nerve conduction parameters alone. Of these 22 patients, 15 were having lower limb neuropathy and 7 were having upper limb neuropathy. So lower limb neuropathy (29.4%) predominates in our study. This finding was similar to the studies done by Singh RB,¹⁵ Salem,⁵ Zhijun¹¹ and Meena.⁷ Among the lower limb neuropathy superficial peroneal nerve was most commonly involved followed by sural nerve and common peroneal and then tibial nerve. Among the upper limb neuropathy median nerve was most commonly involved followed by ulnar nerve. So, while sensory predominates in the lower limb in our study, motor neuropathy predominated in the upper limb. Overall sensory neuropathy was found to be the most common (12%) neuropathy in our study followed by mixed (sensory-motor) neuropathy (6%) and then motor neuropathy (4%). This finding were sensory neuropathy is the most common in diabetics was consistent with the studies undertaken by Bhuyan AK,³ Singh RB,¹⁵ Salem,⁵ Patel,¹⁰ Zhijun.¹¹ Regarding the pathological types of neuropathy, axonal neuropathy predominated in our study (29.4%), followed by mixed (both axonal and demyelinating-9.8%) and then demyelinating (3.9%). This finding was consistent with the study done by Bhuyan AK³ where axonal neuropathy was the most common finding in diabetes patients.

5.4. Associations of SCN in this study

In our study subclinical neuropathy was seen commonly in the age group of 41-60 years as majority of patients involved in this study was in that age group. Male gender was affected more than females with a prevalence of 13%. This finding was consistent with a previous study done by Bhuyan AK,³ Singh,¹⁵ Salem⁵ were male sex of middle age group predominantly had diabetic neuropathy. Coming to the duration of illness, it was found that patients with history of diabetes for more than 5 years was found to have peripheral neuropathy (63.6%) and this finding was statistically significant. So more the duration of diabetes, greater is the risk for developing diabetes related complications and this finding was consistent with the studies undertaken by Salem,⁵ Unmar.¹⁴ Also a higher prevalence of subclinical neuropathy was observed in patients taking oral hypoglycaemic agent for diabetes (91%) compared to those taking insulin or both.

Patients with elevated triglyceride had significant association with subclinical neuropathy and this finding was seen in a previous study done by Unmar.¹⁴ Also patients with elevated fasting blood sugar and postprandial blood sugar had a higher prevalence of subclinical neuropathy at 72% and 86% compared to those with controlled blood sugar values. Also those patients with HbA1C value of more than 6.5% and higher levels were found to have subclinical neuropathy compared to those with a controlled HbA1C values. Nearly half of the cases occurred in those with HbA1C more than 9%. All these findings were statistically significant and was found to be similar to the studies conducted by Bhuyan AK,³ Singh RB,¹⁵ Salem,⁵ Patel¹⁰ and Unmar.¹⁴

6. Conclusion

Nerve conduction study plays a major role in diagnosing early peripheral neuropathy in patients with diabetes mellitus who are asymptomatic for neuropathy with normal clinical examination. In our study nearly 43% of asymptomatic patients had neuropathy which was diagnosed by nerve conduction study. Early diagnosis and adequate control of blood sugar plays the cornerstone of treatment to avoid dreadful complications of diabetic peripheral neuropathy.

7. Limitations

Sample size though being 51 is similar to many studies^{6,9-13} done in the past, is still not adequate enough to rely on the characteristics of neuropathy. So a larger number of patients are required to classify the characteristics of peripheral neuropathy. Type 1 diabetes mellitus patients was not studied in this research due to unavailability of such patients during the study period

8. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

9. Source of Funding

None.

References

1. Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J. Harrison's principle of internal medicine. In: 19th Edn. New York: The McGraw-Hill Companies; 2015. p. 2399–440.
2. Cho NH, Shaw JE, Karuranga S, Huang Y, Fernandes JDR, Ohlrogge AW, et al. Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract.* 2018;138:271–81. doi:10.1016/j.diabres.2018.02.023.
3. Bhuyan AK, Appaiah S. Clinical and electrophysiological correlation of peripheral neuropathy in newly diagnosed type 2 diabetes mellitus. *Int J Adv Med.* 2018;5(3):542–9.
4. Fateh HR, Madani SP, Heshmat R, Larijani B. Correlation of michigan neuropathy screening instrument, united kingdom screening test and electrodiagnosis for early detection of diabetic peripheral neuropathy. *J Diabetes Metab Disord.* 2015;15:8. doi:10.1186/s40200-016-0229-7.
5. Salem KE, Ammari F, Khader Y, Dhaimat O. Elevated glycosylated hemoglobin is associated with subclinical neuropathy in neurologically asymptomatic diabetic patients: a prospective study. *J Clin Neurophysiol.* 2009;26(1):50–3. doi:10.1097/WNP.0b013e31819862ee.
6. Bae JS, Kim BJ. Subclinical diabetic neuropathy with normal conventional electrophysiological study. *J Neurol.* 2007;254(1):253–9.
7. Ahmed HM. Prevalence of nerve conduction abnormalities in type 1 diabetes mellitus. *Clin Neurophysiol.* 2018;129(1):79–80. doi:10.1016/j.clinph.2018.04.198.
8. Maruthi W, Rao R. The role of electrodiagnosis in the evaluation of subclinical diabetic neuropathy. *Ind J Appl Res.* 2015;5(8):451–53.
9. Omer HS, Hamdan FB, Wafi AN. The use of electrophysiological studies in the early diagnosis of subclinical neuropathy in type 2 diabetes mellitus. *Kurdistan Academicians J.* 2008;6(1):1–10.
10. Patel LC, Patel RK. HbA1c- predictor of early peripheral neuropathy in asymptomatic cases of diabetes mellitus. *Int J Basic Appl Physiol.* 2016;5(1):122–5.
11. Zhijun L, Xiaoqing H, Nai T. Significance of Nueroelectrophysiological Tests in the Early Diagnosis of Sub-clinical Neuropathay with Diabetes Mellitus. *J Huazhong Univ Sci Technol.* 2006;26(4):429–31.
12. Devdutt S, Meenakshi S, Rambabu S, Patel B, Kapil G, Jitendra G, et al. Sensory nerve conduction study in non-insulin dependent diabetes mellitus patients with subclinical peripheral neuropathy. *Indian J Appl Res.* 2019;9(11):74–5.
13. Iyagba A, Onwuchekwa A. Diabetes associated peripheral neuropathies. *Int J Med Health Res.* 2016;2(11):29–33.
14. Unmar Y, Zafar MI, Gao F. Factors associated with peripheral neuropathy in type 2 diabetes: subclinical versus confirmed neuropathy. *J Huazhong Univ Sci Technol.* 2017;37(3):337–42.
15. Singh RB, Chandel K, Kumar S. Nerve conduction study findings of subclinical diabetic neuropathy in newly diagnosed diabetic patients. *Ind J Neurosci.* 2015;1(1):1–7.

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