ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 6, Issue – 2, April – 2021 , Page No. : 170 - 177

Study of clinical and electrophysiology of peripheral neuropathy in diabetes

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Citation this Article: Dr. Mansoor, Dr. Omar Farooq, Dr. Showkat Ahmad Kadla, Prof. Samia Rashid, Dr. Javaid A. Basu, Dr. Javeed Ahmad, Dr. Suhail, Dr. Umar Nabi, Dr. Aatif Sanaie, Dr. Mufti Moin, Dr. Mohammad Sayeed, "Study of clinical and electrophysiology of peripheral neuropathy in diabetes", IJMSIR- April - 2021, Vol – 6, Issue - 2, P. No. 170 – 177.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Diabetes has become one of the largest global health-care problems of the 21 century. According to the Centers for Disease Control and Prevention, the population prevalence of diabetes in the US is approaching 10% and is increasing by 5% each year. Diabetic neuropathy is the most common complication associated with diabetes mellitus. There has been an evolution in our understanding of the pathophysiology and the management of diabetic polyneuropathy over the past decade. The purpose of the current study is to evaluate the degree of correlation of clinical examination with electrophysiology in diabetics with peripheral neuropathy for better management of neuropathy in terms of its early and timely detection.

Results ;Most common age group in our study was 70-79 years 26 (27.1%) followed by 25 (26.0%) who belonged to age groups 50-59 and 60-69 years while as 20 (20.8%) belonged to age group < 50 years. The mean age in our study was 59.4 ± 11.83.The minimum age was 37 years and maximum age was 79 years. We assessed the sensitivity and specificity of two major scores NSS and NDS . Sensitivity, specificity, NPV, PPV and accuracy of clinical examination of NSS was 83.33, 66.64, 70.58, 80.64, 66.66;and NDS was 93.93, 52.77, 86.36, 77.02, 69.29 respectively .

conclusion; neurological examination is important for screening neuropathy in diabetics .using different scores like NDS and NSS neuropathy can be predicted with high reliability which can help in early detection and timely management.

Keywords: Centers for Disease Control and Prevention, Diabetes, Peripheral nerve, pathophysiology, polyneuropathy.

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs,

especially the eyes, kidneys, nerves, heart, and blood vessel[1].The diagnosis relies on both clinical signs as well as quantitative testing and may be present despite a lack of reported symptoms[2]. Prevalence of diabetic foot ulcers is around 18.3%[3], and diabetes is a leading cause of lower limb amputation[4]. In addition, neuropathic pain and decreased sensation can contribute to an array of pour outcomes including falls, impaired quality of life, restrictions in activities of daily living, and depressive symptoms[5]. Peripheral neuropathy caused by Diabetes (DM) was recognised only in 1864 by MarcheldeCCalvi. the loss of tendon reflexes in the legs was described by Bouchard (1887)[7] similarities to tabes stressed by Althaus (1885)[8] Based on a modification of the classification proposed by PK Thomas, a number of distinct syndromes are identifiable[9]. Neuropathy in diabetes is a heterogeneous condition that manifests in different forms. It may occur in proximal or distal nerve fibers, may take the form of mononeuritis or entrapments involving small or large fibers, and may affect the somatic or autonomic nervous system[10]. Unfortunately, DPN is often diagnosed late when irreversible nerve injury has occurred and its first presentation may be with a diabetic foot ulcer[11].

Aims and objectives

1. To determine sensitivity of clinical examination in detecting diabetic neuropathy.
2. To determine relation of clinical neuropathy with neuropathy detected on NCV.

Materials and methods

After obtaining the ethical clearance from the Institutional Ethical Committee, the present cross-sectional study was conducted in the Postgraduate Department of Medicine, Government SMHS Hospital an associated hospital of Government Medical College, Srinagar on IPD and OPD patients who were known cases of diabetes mellitus T2DM. This study was done over a period of two years - between May 2018 and December 2020. 96 patients were selected for study. Patients attending outpatient department and inpatient department with history of type 2 diabetes were included after selection criteria.

Inclusion Criteria

- Patients aged >18 years
- Known cases of T2 diabetes mellitus.
- Patient who consent for the study.

Exclusion Criteria

- Patients who are known cases of:
- Chronic renal failure
- Chronic liver failure
- Chronic airway disease
- Carcinoma
- Infection
- Critical illness
- Patients on drugs known to cause peripheral neuropathy.

All the included patients underwent clinical examination followed by nerve conduction stud.

Interpretation of NCV	Axonopathy	Demyelinating
Prolongation of latency	Normal	++
Slowing of NCV	Normal	+
Decrease of amplitude		
CMAP	Decreased	Normal
SNAP	Decreased	Normal
Conduction block	--	+
Temporal dispersion	--	+

Clinical examination includes two scores to be applied to patients

1. Neuropathy symptom score
2. Neuropathy disability score

Assessment of neuropathy: Determination of whether a patient had neuropathy was based on review of the medical record, neurologic tests including bed side autonomic function tests, nerve conduction (NC) abnormalities. Three approaches were used to determine whether a neurologic abnormality was due to diabetes mellitus or to another cause:

1. the patient's history and the medical record were analyzed
2. additional tests were performed if needed; and
3. judgments were made as to whether the findings were typical of diabetic neuropathy.

Systematic questioning, including family history of non-diabetic peripheral nerve disease and the presence of toxic, metabolic, mechanical, and vascular causes of nerve disease, was conducted. All patients underwent tests for complete blood count and routine serum chemistry.

Standardization of examining methods

Patients underwent proper history and physical examination. In the sensory examination ambiguous findings were considered negative. The response to each tests were considered normal, decreased, or absent.

The instruments used were

1. A disposable pin for pain evaluation
2. A cotton tip for light touch
3. A 128 Hz tuning fork for vibration sensation, and

4. Finger and toe movements with immobilization of the proximal joint to evaluate joint position. The sites examined included the distal toe and distal finger. The motor system was examined manually for individual muscles with a previously used validated grading system. Mechanical devices to evaluate strength may not add precision because they emphasize groups of muscles and because the condition of the joints and periarticular tissues frequently are abnormal in diabetes. Muscle testing is of limited value in assessing mild diabetic neuropathy. Weakness appears late and usually only involves intrinsic foot muscles and ankle dorsiflexors; more proximal muscles are only involved in more severe cases of diabetic polyneuropathy.

5. Reflexes were classified as 1) present and active, 2) present and hypoactive, and 3) absent.

Protocol for electrodiagnostic test

A. Motor nerve conduction studies

1. Unilateral studies of ulnar and median nerve including F waves in the upper limb
2. Unilateral studies of peroneal and posterior tibial nerve including F wave in the lower limb
3. Measurement of muscle action potential amplitude and latency at each site of stimulation and calculation of segmental conduction velocity B. Sensory nerve conduction studies.
4. Studies of additional nerves were undertaken to characterize abnormalities based on the distribution of clinical symptoms or signs.
5. The normal values for representative nerve conduction values at various sites of stimulation were derived at after analyzing the NC of 30 age matched patients who came to Neurology OPD for complaints other than neuropathy.

Observation and results

Table 1: Age, gender and duration of diabetes

		No. of Patients	Percentage
Age (Years)	< 50	20	20.8
	50-59	25	26.0
	60-69	25	26.0
	70-79	26	27.1
	Mean±SD (Range)=59.4±11.83 (37-76)		
Gender	Male	40	41.7
	Female	56	58.3
Duration in years	< 5 Years	4	4.2
	5-10 Years	19	19.8
	11-15 Years	23	24.0
	>15 Years	50	52.1

Most common age group in our study was 70-79 years 26 (27.1%) followed by 50-59 and 60-69 years 25 (26%, 26%).There were 20 (20.8%) patients aged <50 years). Female patients were more than male patients with 56 (58.3%) females versus 40 (41.7%) males. Out of 96 patients 50 (52.1%) patients had duration of diabetes >15 years, 23 (24%) patients had duration 11-15 years, 19 (19.8%) had duration 5-10 years and 4 (4.2%) had duration <5 years. most study patients had duration of diabetes more than 10 years and duration of diabetes was considered from the time these patients were labelled diabetic by any medical practitioner.

Table 2: NSS and NDS scores of study patients

		No. of Patients	Percentage
NSS Score (n=96)	0 (Normal)	34	35.5
	3 – 4 (mild)	15	15.6
	5 – 6 (moderate)	31	32.3
	7 – 9 (severe)	16	16.6
NDS Score (n=96)	0 (Normal)	22	22.8
	<5 (Mild)	30	31.3
	6 – 8 (Moderate)	38	39.6
	9 – 10 (Severe)	6	6.3

Out of 96 study patients 62 patients had neuropathy based on NSS score while as 34 patients were found to have no neuropathy (NSS score =0). 15 (15.6%) patients had score of 3-4 (mild), 31 (32.3%) had score of 5-6 (moderate) while 16 (16.6%) patients had a NSS score of 7-9 (severe).

Out of 96 patients 74 patients had neuropathy based on NDS score (NDS SCORE >=1) while 22 patients had no neuropathy (NDS score =0). 30 (31%) patients had NDS

score of <5 (mild), 38 (39.6%) had NDS score of 6-8 (moderate) while as only 6 (6.3%) patients had score of 9-10 (severe).

Determination of sensitivity and specify of clinical examination with respect to nerve conduction studies

Table 3: Correlation of neuropathy ON NSS with neuropathy on NCV				
Neuropathy on NSS SCORE	Neuropathy on NCV		No neuropathy on NCV	
	No.	%age	No.	%age
Yes	50	82.25	12	32.35
No	10	17.74	24	67.64
Total	60	100	36	100
P-value <0.001				

SENSITIVITY =83.33 | SPECIFICITY =66.64 | Diagnostic efficacy=66.666

PPV=80.64 | NPV=70.588

Table 4: Correlation of neuropathy ON NDS with neuropathy on NCV				
Neuropathy on NDS SCORE	Neuropathy on NCV		No neuropathy on NCV	
	No.	%age	No.	%age
Yes	57	91.93	17	51.51
No	3	8.06	19	48.48
Total	60	100	36	100
P-value<0.001				

SENSITIVITY =95.93 | SPECIFITY=52.77 | PPV=77.02 | NPV =86.36 |

Diagonostic accuracy =61.29

Discussion

Most common age group in our study was 70-79 years 26 (27.1%) followed by 25 (26.0%) who belonged to age groups 50-59 and 60-69 years while as 20 (20.8%) belonged to age group < 50 years. The mean age in our study was 59.4±11.83. The minimum age was 37 years and maximum age was 79 years. Our results were similar to the study conducted by **Mohan G et al**[12] where the mean age was 57.90 years and minimum and maximum age was 31 and 91 years. The mean age at which neuropathy started in our diabetic population was 52 years. In our study the prevalence of diabetic neuropathy was maximum in the age group 70 to 79 years. The prevalence of diabetic neuropathy is associated with age as has been depicted in study conducted by **Won JC et al**[13]where they found increase in age is an independent risk factor for diabetic neuropathy and prevalence of DPN with increase in age. Our results were also consistent with findings in a study done **Zoungas S et al (2014)**[14] wherein increase in the age was associated with increase in micro and macrovascular complications.

The current study enrolls more female patients 56 (58.3%) than male patients 40 (41.7%), this difference might be due to more prevalence of neuropathic symptoms in female patients than in male patient as has been shown in a study conducted by **Abbott CA et al**[15] where 15692 cases were assessed and they found 38%

of females reported painful symptoms versus 31% males.

Out of 96 patients 50 (52.1%) patients had du-ration of diabetes >15 years, 23 (24%) patients had duration 11-15 years, 19 (19.8%) had duration 5-10 years and 4 (4.2%) had duration <5 years. **Soheilykhah S et al**[16] conducted a study the prevalence of diabetic neuropathy was shown to be 59% in which 33.5% had duration of diabetes of more than 15 years.

Out of 96 study patients 62 (64.8%) patients had neuropathy based on NSS score while as 34 patients were found to have no neuropathy (NSS score =0). Out of 96 patients 74 (77%) patients had neuropathy based on NDS score (NDS SCORE >=1) while 22 patients had no neuropathy (NDS score =0). On NSS grading, 34 patients were found to have no neuropathy (NSS score =0). 15 (15.6%) patients had score of 3-4 (mild), 31 (32.3%) had score of 5-6 (moderate) while 16 (16.6%) patients had a NSS score of 7-9 (severe).Based on NDS grading score, 22 patients had no neuropathy (NDS score =0). 30 (31%) patients had NDS score of <5 (mild), 38 (39.6%) had NDS score of 6-8 (moderate) while as only 6 (6.3%) patients had score of 9-10 (severe). **Bhuyan AK et al**[17] conducted a study in which prevalence of neuropathy was found to be 68.75% based on abnormal NSS, NDS, NCS, the results of the study closely resemble our findings**.** Similar results were obtained by **Mohan G et al**[13], in their study 80 patients were included with mean age of diagnosis of diabetes being 47 years. As per NSS grading, 29% of their patients were normal, 11% had mild neuropathy, 33% had moderate neuropathy while as 27% had severe neuropathy. On NDS score, 44% patients were normal, 9% patients had mild neuropathy, 42% patients had moderate neuropathy while as 5% had severe neuropathy.

We assessed the sensitivity and specificity of two major scores i.e NSS and NDS taking NCS as gold standard. Taking the two closest studies regarding the protocol taken from the above mentioned report, the results of our study were compared with an Indian study by **Bansal V et al**[18] that also suggested the use of NCS to assess the validity of other diagnostic tests for diagnosing DPN, NDS was found to be reliable regarding sensitivity. They have found that NDS is 92% sensitive and 48% specific.. However in another study by **Gentile et al**[19] the clinical examination was found to be 94% and 92% sensitive and specific respectively taking NCS as reference.

In our study we found the sensitivity, specificity, NPV, PPV and accuracy of clinical examination of NSS 83.33, 66.64, 70.58, 80.64, 66.66; and NDS 93.93, 52.77, 86.36, 77.02, 69.29 respectively. These findings are similar to the study conducted by **Asad et al**.[20]

Summary

1. In our study mean age of distribution was 59.4±11 years, maximum number of patients were in age group included 70-79.
2. Our study included more female patients than male patients 56 female and 40 male patients.
3. Mean duration of diabetes was 14.3 years.
4. On NSS grading, 34 patients were found to have no neuropathy (NSS score =0). 15 (15.6%) patients had score of 3-4 (mild), 31 (32.3%) had score of 5-6 (moderate) while 16 (16.6%) patients had a NSS score of 7-9 (severe).
5. Based on NDS grading score, 22 patients had no neuropathy (NDS score =0). 30 (31%) patients had NDS score of <5 (mild), 38 (39.6%) had NDS score of 6-8 (moderate)

while as only 6 (6.3%) patients had score of 9-10 (severe).

6. With age electrophysiological abnormalities increase in diabetic patients.
7. With increase in the duration of diabetes the prevalence of neuropathy increases.
8. Symmetrical neuropathy was the most common type of neuropathy found on clinical examination as well as on Electrophysiology. The prevalence of symmetrical neuropathy in our diabetic population was 48% on NSS and 35% on electrophysiology.
9. Diabetic neuropathy can be asymptomatic and can be detected in routine examination of patients during visits to medical practitioners or can even be missed on clinical examination and only detected by electrophysiology.
10. Patient who are diabetic should undergo neurological examination directed to detect peripheral neuropathy as well as electrophysiology.
11. Sensitivity, specificity, NPV, PPV and accuracy of clinical examination (NSS 83.33, 66.64, 70.58, 80.64, 66.66; NDS 93.93, 52.77, 86.36, 77.02, 69.29).

Conclusion

Diabetic neuropathy constitutes a high burden of disease in diabetics leading to many serious health consequences. Patient who are diabetic should undergo neurological examination directed to detect peripheral neuropathy as well as electrophysiology. Patients should undergo periodic assessment of neuropathy, annual screening as many diabetics do not have symptoms of neuropathy only detected by nerve conduction studies. Of diabetic should be carried out to avoid complications of diabetes like diabetic foot which can be prevented by early detection of neuropathy. Neurological examination is important for screening neuropatrhy in diabetics, using different scoring systems as NDS and NSS can predict neuropathy in diabetics with high reliability and help in timely detection and management of neuropathy.

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