Nerve conduction study findings of subclinical diabetic neuropathy in newly diagnosed diabetic patients

Ram Babu Singh[1], Kuldeep Chandel[2], Sudhir Kumar[3]

[1,2]Assistant Professor, Department of Medicine, [3]Professor, Department of Plastic Surgery, Maharani Laxmi Bai Medical College, Jhansi

Corresponding Author:
Ram Babu Singh
Assistant Professor, Department of Medicine, Maharani Laxmi Bai Medical College, Jhansi
Email: dr.rbsjhansi@gmail.com

Abstract

Background: *Diabetes induced neuropathy is one of the most challenging complication of diabetes mellitus and is one of the major causes of non-traumatic limb amputation. The exact prevalence of diabetic neuropathy is not known and reports shows variable prevalence. There are good number of patients, who have subclinical neuropathy at the time of detection of diabetes.*

Aim: *He aim of this study was to investigate the prevalence of subclinical neuropathy in newly diagnosed diabetic patients.*

Methods and Material: *In this study, 104 diabetic patients and 50 healthy subjects have been studied prospectively during 2011 - 2012, in OPD of Department of Medicine, M.L.B. Medical college, Jhansi. All patients were clinically asymptomatic. At least one abnormal independent neurophysiological nerve parameters, which were required as the criterion of the peripheral nervous system sub clinical involvement, following results were drown.*

Results: *The mean MNCV was significantly lower in the diabetic group (39.0 ± 5.0 m/s) when compared with non-diabetic controls (53 ± 4 m/s; P=0.0001). The mean SNCV value of case (44.05+/-11.8 m/s) and control (46+/-5 m/s) had no significant difference(p value=.37). In motor nerve conduction studies, the distal motor latency (DML) is most frequent abnormal parameter in studied nerves of upper limbs, while mean f, and MNCV is the most frequent abnormality in lower limb nerves. In all sensory nerve conduction study, the most frequent abnormal parameter was the onset of latency.*

Conclusion: *We conclude that the percentage of abnormal electrophysiological parameter in different motor and sensory nerve were 77% in sural nerve, 66% in peroneal nerve, 63.4% in posterior tibial nerve, 57% in median motor nerve, 46.6% in ulnar motor nerve, 40% in median sensory nerve, and 47% in ulnar sensory nerve. Thus, the incidence of subclinical neuropathy is significantly higher in newly detected diabetics in this study.*

Key word: *Nerve Conduction, Subclinical Diabetic Neuropathy*

Introduction

Diabetic neuropathy (DN) is an important complication of diabetes mellitus, leading to the high morbidity besides huge cost involve in treatment. It invokes physical and mental trauma to patients and his nearer ones and also involve doctors of several specialties. It is also responsible for 50-75% of non-traumatic amputation[1]. D.N. is a set of clinical syndromes that affect distinct regions of the nervous system. It may be silent and go undetected or it may present with clinical symptoms and signs that are nonspecific and insidious with slow progression.

The true prevalence is not known and reports vary from 10% to 90% in diabetic patients, depending on the criteria and methods used to define neuropathy. According to Dyck PJ ET al[2], Twenty five percent of patients attending a diabetes clinic volunteered symptoms; 50% were found to have neuropathy after a simple clinical test such as the ankle jerk or vibration perception test; almost 90% tested positive to sophisticated tests of autonomic function or peripheral sensation. Neurological complications occur equally in type 1 and type 2 diabetes mellitus and additionally in various forms of acquired diabetes. The major morbidity associated with somatic neuropathy is foot ulceration, the precursor of gangrene and limb loss. Neuropathy increases the risk of amputation 1.7 fold; 12 fold, if there is deformity (itself a consequence of neuropathy), and 36 fold, if there is a history of previous ulceration.

This study is aimed to determine the situation of the deferent nerve fiber types and the prevalence of subclinical neuropathy in type 1 & 2 diabetes mellitus, who are first time diagnosed and do not complain of any clinical symptoms.

Material and Methods

A total 104 random patients of newly diagnosed type-1& type-2 diabetes mellitus were studied, who were attending the OPDs of department of medicine at M.L.B. Medical College, Jhansi during 2011- 2012. Informed consent prior study were taken from all the subjects (Group I). Control (Group II) group consist of patient's relatives and volunteers of similar age & sex with similar nutritional status but without any obvious cause of neuropathy.

Complete history and physical examination of the cases were done. In history symptoms of autonomic dysfunction and peripheral neuropathies were included such as Tingling, numbness or pain the toes, feet legs, fingers, hands and arms, wasting of the muscles of the feet or hands, indigestion, nausea or vomiting, diarrhea or constipation, Dizziness or faintness, Problem with urination and erectile dysfunction (impotence), Vaginal dryness, Weakness, weight loss or depression.

During neurological examination patients were examined as per Diabetic Neuropathy Examination, a scoring system for distal polyneuropathy, for determining the presence and severity of distal symmetrical polyneuropathy. **(Rochester Diabetic Neuropathy Study, 1997)[3]**

DNE (Diabetic Neuropathy Examination): This is a modified form of neuropathy disability score (NDS)[4]. NDS is a widely accepted and validated physical examination scoring system, with 8 items used to diagnose neuropathy.

DNE is a scoring system with 8 items. It is sensitive, fast and easy to perform in clinical practice.

1. **Muscle strength**: **Quadriceps femoris**: extension of the knee; **Tibialis anterior**: dorsiflexion of the foot
2. **Reflex**: Ankle jerk
3. **Sensation index finger**: Sensitivity of pinpricks
4. **Sensation: big toe**: Sensitivity to pin pricks, Sensitivity to touch, Vibration perception, Sensitivity to joint position

Only the right limbs are tested scoring done from 0 to 2:

0 = normal

1 = mild/moderate deficit, Muscle strength: Medical Research Council scale >3-4.

- **Reflex:** decreased but present
- **Sensation:** decreased but present.

2 =

- severely disturbed/absent
- Muscle strength: Medical Research Council scale< 3-4
- Reflex: absent
- Sensation: absent

Maximum score: 16 points. At a cutoff point of 3 to 4, the sensitivity and specificity of the DNE were 97% and 59% respectively,

Monofilament Test: This test was meant to assess the sensory status of foot. This test was done with 10gm Semmes-Weinstein monofilament. Monofilament was touched at different sites of foot on plantar aspect of metatarsal heads, plantar are of heel and dorsal aspect of mid foot. Monofilament was pushed hard enough to make the filament bend and patients were asked whether they could appreciate the sensation of touch or not. Table 1 & 2 shows the normal values of electrophysiological study values.

Table 1: Motor nerve conduction studies

Motor nerve conduction studies				
Nerve	**Onset Lat. (ms)**	**AMP(mV)**	**CV(m/s)**	**F-Wave Lat.(ms)**
Median	<4.2	>4.4	>49	<31
Ulnar	<3.4	>6.0	>49	<32
Radial	<5.2	>4.0	>50	NA
Peroneal	<5.8	>2.0	>42	<58
Tibial	<6.5	>3.0	>41	<59

Table 2: Sensory nerve conduction studies

Sensory nerve conduction studies				
Nerve	**Onset lat. (ms)**	**Peak lat. (m/s)**	**Amp. (μ v)**	**CV(m/s)**
Median	<2.5	<3.5	>20	>52
Ulnar	<2.1	<3.0	>15	>52
Radial	<1.9	<2.8	>20	>48
Sural	<3.2	<4.4	>6	>42

Table 3: Distribution according to type of diabetes

Type of Diabetes	**Male**		**Female**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Type I	5	4.8	4	3.84	9	8.65
Type II	61	58.65	34	32.69	95	91.34

Table 4: Showing routine investigations of cases and controls

Variables	**Newly diagnosed diabetics (Mean+/SD) (n=104)**	**Non diabetics controls (Mean+/SD) (n=50)**	**P value**
Age	42.29+/-16.22	43.42_/-13	.33 NS
FBS	213.98	97+/-12	**.0001**
PPBS	214.08	110+/-18	**.0001**
HbA1c	7.89+/-1.5	5.6+/-.5	**.0001**
S. Lipid profile			
1. Triglyceride (mg %)	255+/-10 132+/-12	248+/-8 124+/-40	**.0001**
2. LDL (mg %)	212+/-48 52+/-10	202+/-43 55+/-5	.06 NS
3. Cholesterol (mg %)	31.64+/-7.6	30+/-4	.212 NS
4. HDL (mg %)	.94+/-.26	.8+/-.1	.04
S. Urea	4.8%	1.8%	.54 NS
S. Creatinine	4.78%	1.8%	.06 NS
Fundus retinopathy	6%	5%	NS
Micral test(spot sample)			NS
NCS:			
MNCV(m/s)			
SNCV(m/s)	39.475+/-5.25	53+/-4	**.0001**
	44.45+/-11.8	46+/-5	.37NS

Criteria for Exclusion of subject:

1. Patients having diabetes with clinical symptom of diabetic neuropathy.
2. Patients with family history of inherited neuropathy, occupational or Environmental history of heavy metal exposure, history of lumbar or cervical radiculopathy as well as patients using medication which could cause polyneuropathy was excluded.
3. Seriously ill or comatose patients would be excluded from the study.

Observation and results

Out of total 104 patients, there were 9(8.65%) type I and 95(91.34%) were type II diabetics. Among type 1, 5(4.80%) patients were males and 4(3.84%) were females. Among type 2, 61(58.65%) are males and 34(32.69%) are females (Table 3).

Age, S. Urea, S. Creatinine, sensory nerve conduction velocity, urine micro-albumin test and retinopathy in diabetic patients did not differ significantly (P value>.05) with control group. But two other important parameters HbA1c level and motor nerve conduction velocity were significantly differ in (p value< .05) diabetic group when compared with non-diabetics controls. Mean value of HbA1c level was significantly higher in diabetic group (7.89+/-1.5) as compared to non-diabetic control (5.6+/-.5, p-value was .0001). The motor nerve conduction velocity was significantly low in diabetic group (39.47+/-5.25) as compare to non-diabetic control (53+/-4, p value.001). While comparing S. Lipid

profile the triglyceride level was significantly higher in diabetic group (255+/-10) as compared to non-diabetic controls (248+/-8, p value=.0001). The HDL level was significantly lower in diabetic group (52+/-10) as compared to non-diabetic controls (55+/-5, p value=.04), but LDL level and S. Cholesterol level were not differ significantly (p value >.05). (Table 4)

On comparing the mean value of the motor and sensory latencies, Compound muscle action potentials (CMAP), motor conduction velocities (MNCV) & sensory nerve conduction velocities (SNCV) for median, ulnar, peroneal, tibial & sural nerves and Mean distal motor latency (DML) between cases and controls, CMAP and MNCV were significantly deferent in diabetic group for median nerve (p<.05), the mean values are 7.49+/-2.6, 7+/-7.6, 40+/-15 respectively for diabetic group & 3.6+/-.4, 12+/-3.8 & 54.8+/-4.6 respectively for control group.

There was no significant difference in mean F Wave latency of studied median nerve in case & control group. The mean value was 28.74+/-12.3 m & 26.7+/-6.5 respectively.

The Distal motor latency, MNCV, mean F wave latency of studies ulnar nerve were 6.12+/-3.8, 45.74+/-11.4 & 33.23+/-15 diabetic group and was differ significantly (p value <.05) when compare with control group.

The mean value of distal motor latency & CMAP for studied tibial nerve was comparable to those from control group, but there was significant difference in mean value for MNCV & mean F.

The mean value of distal motor latency & mean F wave latency of peroneal nerve were comparable with control group, but there was significant difference in mean value of CMAP & MNCV.

Table 5: Comparison of motor nerve conduction parameters between the patients and control group

Parameters	Patient group Mean+/-SD	Control group Mean+/-SD	P value
Median nerve			
DML(ms)	7.49+/-2.6	3.6+/-.4	.0001
CMAP(mv)	7.0+/-7.6	12/-3.8	.0001
MNCV(m/s)	40.15+/-15	54.8+/-4.6	.0001
Mean F(ms)	28.74+/-12.3	26.7+/-6.5	.273 NS
Ulnar nerve			
DML(ms)	6.12+/-3.8	2.8+/-.1	.0001
CMAP(mv)	6.47+/-8.2	7.1+/-5	.61 NS
MNCV(m/s)	45.74+/-11.04	58+/-8	.0001
Mean F(ms)	33.23+/-15	26.8+/-1.3	.0103
Tibial nerve			
DML(ms)	6.35+/-3.46	5.8+/-3	.34 NS
CMAP(mv)	5.46+/-4.6	6.5+/-3.6	.14 NS
MNCV(m/s)	36.8+/-10	47+/-1.9	.0001
Mean F(ms)	58.49+/-61	48.5+/-1.8	.001
Peroneal nerve			
DML(ms)	5.87+/-2.9	4.9+/-3	.056 NS
CMAP(mv)	3.68+/-3.23	7.5+/-2.6	.0001
MNCV(m/s)	34.44+/-12.52	47+/-1.9	.0001
Mean F(ms)	50.28+/-18	48.5+/-10	.515 NS

While comparison of sensory nerve conduction parameters in patients & control group. There was significant difference in mean value of Distal sensory latency, SNAP & SNCV for studied sural nerve, the mean value of diabetic group was 2.9+/-.4, 5.40+/-2.2, & 36.45+/-12 and for non-diabetic controls was 2.8+/-.1, 9.3+/-2.3 & 44.1+/-3.5 respectively and supposed to be most frequent involved nerve in diabetic patients. The mean value of SNAP was comparable for both case (23.29+/-15.6 & 16.65+/-4.4) and control (26.1+/-10 & 22.2+/-9.4) group of studied median and ulnar nerve, but there was significant difference in mean sensory conduction velocities of case (44.72+/-18, 38.78+/-3.4) and control (55+/-2.2, 55+/-4.4) with p value<.05 (Table 6).

Table 6: Comparison of sensory nerve conduction parameters between case and control group

Parameter	Patient group (n=105) mean+/-SD	Control group (n=50) mean+/-SD	P-value
Median sensory nerve			
DSL(ms)	2.7+/-.2	2.5+/-.1	.002
SNAP(micV)	23.29+/-15.6	26.1+/-10	.24 NS
SNCV(m/s)	44.72+/-18	55+/-2.2	.0001
Ulnar sensory nerve			
DSL(ms)	2.6+/-.2	2.5+/-.2	.23 NS
SNAP(micV)	16.65+/-44	22.2+/-9.4	.37 NS
SNCV(m/s)	38.78=/-34	55+/-4.4	.001
Sural nerve			
DSL(ms)	2.9+/-.4	2.8+/-.1	.008
SNAP(micV)	5.40+/-2.2	9.3+/-2.3	.0001
SNCV(m/s)	36.45=/-12	44.1=/-3.5	.0001

For median and ulnar nerve study Distal motor latency (57.6% & 46.6%) was the most frequent abnormal parameter, While CMAP is abnormal in 41% and 20% cases respectively.

Other frequently abnormal parameter are MNCV in 23%, 43% in median and ulnar nerve. F wave latency was abnormal in 17% & 43% cases. In peroneal and posterior tibial nerve study mean F latency is abnormal in 66.6% and 63.4% cases MNCV abnormal in 70% & 60% of cases CMAP abnormal in 34% & 30%, Distal motor latency was abnormal in 24% & 20% cases.

The frequency of abnormalities assessed for sensory nerve conduction studies the sural nerve was the most frequently abnormal sensory nerve, abnormal conduction parameter was DSL in 77% cases, SNAP in 20% cases SNCV in 23% cases. (Table 7)

Table 7: Percentage of abnormalities in the studied nerve conduction parameter of studied

	Parameter	Abnormal(mean+/-SD)	N=pt. with abn. parameter	%
Median nerve	DML (ms)	8.34+/-2.3 6.65+/-	59	57.6
	CMAP (mV)	5.4 38.4+/-12	43	41
	MCV (m/s)	31+/-12.2	24	23
	Mean F	21+/-12	17	17 40
	SNAP (uV) SNCV(m/s)	40.7+/-2	42	20
			21	
Ulnar nerve	DML (ms)	6.5+/-2.4	48	46.6 20
	CMAP (mV)	7+/-8	21	43 47
	MEAN F	44.2+/10	45	30
	MCV (m/s)	34+/-14	49	30
	SNAP (uV) SNCV(m/s)	17.5+/-41	31 31	
		40.8+/-22		
Tibial nerve	DML (ms)	6.4+/-3	21	20
	CMAP (mv)	5.2+/-3	31 62	30
	MCV (m/s) MEAN F	35+/-8	66	60
		59+/-45		63.4
Peroneal nerve	DML (ms)	6+/-2	25 35	24
	CMAP (mV)	3.5+/-2	73 67	34
	MCV (m/s)	33+/-12		70
	MEAN F	51+/-13		66.6
Sural nerve	DSL	3.4+/-.2	80	77
	SNAP (uV)	5.2+/-2	21 24	20
	SNCV	32.8+/-11		23

Discussion

The present study focused on a group of newly diagnosed diabetic patients who were neurologically normal. Recommendations for standardized classification of diabetic neuropathy made by the American Diabetic Association and Academy of Neurology include measurement of at least one parameter of nerve conduction studies. The sub clinical diabetic neuropathy has been defined as the presence of nerve lesions attributable to diabetes mellitus in the absence of abnormal clinical data but detectable through electrophysiological studies. In our study the cases are newly diagnosed diabetic patients.

The affected nerve conduction parameters in our diabetic group were the distal latencies and conduction velocities, whereas the amplitudes of sensory and motor responses were not significantly different from the control. This suggests that the early diabetic effects on the peripheral nerves are mainly demyelinating[7].

It is notable that the percentage abnormality of affected nerves in our series was 77% in sural nerve, 66.6% in peroneal nerve, 63.4% in posterior tibial nerve, 57% in median motor nerve, 46.6% in ulnar motor nerve, 40% in median sensory nerve, and 47% in ulnar sensory nerve. Our findings are well correlated with the done by **S. Kersidag el al[8],** who found that sural nerve affected in 86.7% cases, peroneal nerve in 83.3%, posterior tibial motor nerve in 73.3%, median motor nerve in 66.7%, ulnar motor nerve in 63.3%, median sensory nerve in 60%, and ulnar sensory nerve in 46.7% cases. **Dyck et al.[9]** found that the peroneal motor nerve had highest abnormality, followed by the sural nerve, median sensory and median motor nerve, In our study, the most affected nerve were the sural sensory nerve, peroneal motor nerve, posterior tibial motor nerve, median motor nerve, ulnar motor nerve, median sensory nerve, and ulnar sensory nerve in descending order. On comparing studies performance in middle east Asia by **Abdulsalam A et al[10]**, the electrophysiological findings in patients with newly diagnosed non-insulin-dependent diabetes mellitus (NIDDM), twenty-nine patients (22 males, 7 females, mean ages 47 and 37 years, respectively) were studied within four weeks of establishing the diagnosis. They were all given nerve conduction studies by the same examiner. Comparison was made with data from a group of 64 normal control subjects. The electromyogram examination was performed on 24 patients and showed evidence of denervation and/or chronic reinnervation in seven (29%). The frequency of abnormalities in the studied peripheral nerves was 60% for median, 63% ulnar, 33% peroneal, 16% tibial and 8% sural.

After evaluating the results we suggested that the most useful and practical nerves for the electrophysiological study in diabetic patients were the motor and sensory nerves in lower extremity. The nerve dysfunction in lower extremity must be correlated with the length of the nerves. All necessary proteins which are synthesized in cell body are transmitted to distal parts of nerve by axoplasmic flow and maintain the anatomic and functional integrity of the nerve. The interruption of axoplasmic flow in long nerve is more prominent than in short nerves. So data indicate that in early period the axoplasmic flow might have been affected.

In recent years, the value of F response determination in diabetic polyneuropathy has been elicited. The f wave assessment is suitable in the evaluation of proximal motor conduction.

Our findings point out that the dysfunction of some parameters like distal latency in upper extremity is more extensive and this showed us that the nerve dysfunction is more frequent distally. Because these nerves are shorter conduction disorder due to the affection of the axoplasmic flow is more prominent distally. The high frequency of the dysfunction of nerve conduction velocity and F parameter in long nerve of lower extremity is related to slow conduction in the proximal part of nerve. Conduction abnormalities are more frequent in large myelinated fibers in early stage of diabetes but there is also prominent involvement in small myelinated and unmyelinated fibers especially in lower extremity. Thus nerve length might be an important factor in early dysfunction of nerve. In our study we find that the somatic large fibers could be affected in early stage of diabetes.

Summary and Conclusion

- The mean MNCV was significantly lower in the diabetic group (39.41 ± 5.25 m/s) when compared with non-diabetic controls (53 ± 4 m/s; *P*=0.0001).
- The mean SNCV value of case (44.45+/-11.8

m/s) and control (46+/-5 m/s) had no significant difference(p value=.37).

- The distal motor latency (DML) is most frequent abnormal parameter in studied nerves of upper limb, i.e. 57.6% & 46.6% cases had abnormal DML in median and ulnar nerve respectively, while mean f, and MNCV is the most frequent abnormality in lower limb nerves i.e. tibial (63.4%, 60%) & peroneal nerve (66.6%, 70%). In all sensory nerve conduction study, the most frequent abnormal parameter was the onset of latency.
- Based on criterion of the peripheral nervous system sub clinical involvement, the percentages of abnormal electrophysiological parameter in different motor and sensory nerve were 77% in sural nerve, 66.6% in peroneal nerve, 63.4% in posterior tibial nerve, 57% in median motor nerve, 46.6% in ulnar motor nerve, 40% in median sensory nerve, and 47% in ulnar sensory nerve.

The correlation analysis showed that there was no difference in mean MNCV & SNCV value between males (MNCV: 41.5 m/s SNCV: 41.25m/s) and females (MNCV: 40.5 m/s SNCV: 41.5m/s) in diabetic group as well as there was no significant difference in mean value of nerve conduction parameter between type I and type II diabetic patients.

The present study showed that the incidence of subclinical neuropathy was found to be significantly higher in newly detected diabetic patients. Thus it is important to evaluate all newly detected diabetics, for subclinical neuropthy and incorporation of electrophysiological study as routine test.

Abbreviations

DN= Diabetic neuropathy, **NCV=** Nerve Condunction Velocity, **MNCV=** Motor Nerve Conduction Velocity, **SNCV=** Sensory Nerve Conduction Velocity, **DNE=** Diabetic Neuropathy Examination, **NDS**= Neuropathy Diabetic Score

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