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Original article

# Cross sectional study to evaluate the effect of duration of type 2 diabetes mellitus on the nerve conduction velocity in diabetic peripheral neuropathy

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ABSTRACT

*Objective:* To study the nerve conduction velocity in clinically undetectable and detectable peripheral neuropathy in type 2 diabetes mellitus with variable duration.
*Material and methods:* This cross sectional study was conducted in diagnosed type 2 diabetes mellitus patients. They were divided in groups: Group I ($n = 37$) with clinically detectable diabetic peripheral neuropathy of shorter duration and Group II ($n = 27$) with clinically detectable diabetic peripheral neuropathy of longer duration. They were compared with T2DM patients ($n = 22$) without clinical neuropathy. Clinical diagnosis was based on neuropathy symptom score (NSS) and neuropathy disability score (NDS) for signs. Nerve conduction velocity was measured in both upper and lower limbs. Median, ulnar, common peroneal and posterior tibial nerves were selected for motor nerve conduction study and median and sural nerves were selected for sensory nerve conduction study.
*Results:* The comparisons were done between nerve conduction velocities of motor and sensory nerves in patients of clinically detectable neuropathy and patients without neuropathy in type 2 diabetes mellitus population. This study showed significant electrophysiological changes with duration of disease. Nerve conduction velocities in lower limbs were significantly reduced even in patients of shorter duration with normal upper limb nerve conduction velocities.
*Conclusion:* Diabetic neuropathy symptom score (NSS) and neuropathy disability score (NDS) can help in evaluation of diabetic sensorimotor polyneuropathy though nerve conduction study is more powerful test and can help in diagnosing cases of neuropathy.


## 1. Introduction

Diabetic peripheral neuropathy (DPN) is the most commonly reported long-term diabetic complication, affecting up to 50% of type 2 diabetic patients (T2DM) [1]. Developing in patients with diabetes, it is known to be heterogenous by their symptoms, pattern of neurologic involvement, course, risk covariates, pathologic alterations and underlying mechanism [2,3]. Neuropathy may be silent and may go undetected while exercising its ravages or it can manifest with clinical symptoms and signs that mimic those seen in many other diseases. The typical DPN is a chronic, symmetrical, length – dependent sensory motor polyneuropathy [2]. Distal symmetrical sensorimotor polyneuropathy is the most common type of diabetic neuropathy. It involves both small and large fibers and has an insidious onset. Typically, the most distal parts of the extremities are affected first, resulting in a stocking pattern of sensory loss [4]. As the sensory symptoms advance distal upper limbs and later the anterior aspect of trunk get involved. The primary risk factor for diabetic neuropathy is hyperglycemia [5]. The duration of diabetes also increases the risk of neuropathy, but the association between duration and prevalence may depend in part upon patient age, which itself is a risk factor [5,6]. The sensory symptoms and signs are more common than motor symptoms and signs. Its symptoms are extremely variable, ranging from severely painful symptoms at one extreme to the completely painless variety, which may present with an insensitive foot ulcer at the other end. As the feet lose sensation, the risk of trauma and the impaction of foreign objects become a danger leading to diabetic foot. DPN is a major contributory factor to foot ulceration and also amputation [7]. Thus, screening and appropriate treatment for DPN are of paramount importance. The aim of this study was to evaluate the method to detect neuropathy at earliest stage.

## 2. Materials and methods

### 2.1. Study design

The study was conducted in Rajeev Gandhi Centre for Diabetes and Endocrinology and Department of Physiology on patients of

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type 2 diabetes mellitus attending diabetes clinic during year 2011–2012 after approval from the ethical committee of Medical College. Design of the study was cross sectional and only T2DM patients were assessed for diabetic peripheral neuropathy.

### 2.2. Inclusion criteria

- Only T2DM patients aged 30–69 years.
- The diagnosis of diabetes was made on the basis of revised American Diabetes Association Criteria, that, fasting plasma glucose $\geq$126 mg/dl ($\geq$6.1 mmol/l) and 2 h postprandial plasma glucose $\geq$200 mg/dl ($\geq$11.1 mmol/l).
- Possible neuropathy in diagnosed T2DM patients.
- Informed consent for nerve conduction study.

### 2.3. Exclusion criteria

- No previous history of any systemic condition related to peripheral neuropathy (malnutrition, alcoholic neuropathy, renal failure).
- Any neuromuscular diagnosis, such as myopathy, familial polyneuropathy or chronic polyneuropathy or GB syndrome.
- Trauma in the course of nerve to be examined.
- Neuropathies associated with exogenous toxins, metals, or drugs.
- Skin lesions or swelling that would interfere with nerve conduction.

### 2.4. Clinical data collection and examination

Patients general information such as gender, age, diabetes duration, height, weight waist circumference and hip circumference were obtained through proper history and examination as per pre-designed proforma. Body mass index (BMI) [weight (kg)/height (m)$^2$]and waist hip ratio[WC (cm)/HC (cm)] were calculated. Patients with symptoms of paraesthesia/burning/numbnesss/tingling/cramping/aching were assessed on basis of neuropathy symptom score (NSS) and clinical examination for neuropathy disability score (NDS). Neuropathy symptom score consisted of score 2 for Burning/numbness/tingling or 1 for fatigue/cramping/aching. Further score for localization was added as 2 for feet/1 for leg/0 for elsewhere. Then score for exacerbation or symptom improvement was added. Maximum possible score was 9 and the patients having score $\geq$3 were regarded as clinical peripheral neuropathy. Neuropathy disability score (NDS) was based on four tests: vibration perception test, temperature perception on dorsum of foot, pin-prick and Achilles reflex. Assessment of vibration sensation was done using 128-Hz tuning fork tested over the tip of the great toe bilaterally. The response was considered abnormal when the patient lost vibratory sensation while the examiner still perceived it. Temperature perception was tested by cold sponge to see the cold temperature perception. Inability to perceive pin-prick just proximal to the toe nail on the dorsal surface of the hallux, would be regarded as an abnormal test result. Ankle reflex was assessed with a tendon hammer and was recorded as either present or absent. Total absence of ankle reflex either at rest or upon reinforcement was regarded as an abnormal result.

All neuropathy patients were divided in two groups based on duration of T2DM.

Group I ($n$ = 37) with less than 8 years and
Group II ($n$ = 27) with equal to or more than 8 years.

The findings were also compared with group of 22 age, sex and BMI matched T2DM patients without clinical neuropathy.

### 2.5. Blood sampling and biochemical assay

Selected patients were asked to report endocrinology laboratory after an overnight fasting of 10–12 h in fasting state for all baseline investigations. Blood samples were collected in EDTA–Na vials for estimation of glycosylated hemoglobin $HbA_{1C}$, fluoride vials for plasma glucose, in plain vials for serum lipids and lipoproteins, serum creatinine. Spot blood samples for fasting glucose and postprandial glucose were collected on same day.

Plasma glucose was measured by glucose oxidase peroxidase enzymatic method. Estimation of glycosylated hemoglobin ($HbA_{1C}$) was done by cation exchange resin method (reagent supplied by Pointe Scientific Inc. Michigan, USA) and serum creatinine by Jaffe Manners Method. Serum triglycerides, HDL cholesterol, and total cholesterol were measured by enzokits, Ranbaxy diagnostics and cholesterol reagent set supplied by Pointe Scientific Inc., Michigan, USA. Serum LDL cholesterol concentration was calculated indirectly by using Friedwalds equation:

$$\text{LDL} = \frac{\text{total cholesterol} - \text{HDL conc} - \text{triglycerides}}{5}$$

### 2.6. Measurement of nerve conduction velocity

Nerve conduction velocity measurement was performed using Neuroperfect software on windows based computerized EMG/NCV/EP system supplied by Medicaid System, Chandigarh, India.

Nerve conduction velocities were measured with standard surface stimulating and recording techniques. Electrodes were coated with electroconductive gel and held in place with adhesive tape. Nerve conduction velocity was measured in both upper and lower limbs bilaterally. Median, ulnar, common peroneal and posterior tibial nerves were selected for motor nerve conduction study and median and sural nerves were selected for sensory nerve conduction study.

Motor NCV was measured by electrical stimulation of a peripheral nerve and recording from a muscle supplied by this nerve. The time it takes for the electrical impulse to travel from the stimulation to the recording site was measured. This value was called the latency and was measured in milliseconds (ms). By stimulating in two different locations along the same nerve, the NCV across different segments could be determined. Calculations were performed using the distance between the different stimulating electrodes (mm) and the difference in latencies (ms) and ratio is depicted as nerve conduction velocity (m/s).

Sensory NCV was measured by electrical stimulation of a peripheral nerve and recording from a purely sensory portion of the nerve, such as on a finger. The recording electrode is the more proximal of the two. Like the motor studies, sensory latencies were on the scale of milliseconds. The sensory NCV was calculated based upon the latency and the distance between the stimulating and recording electrodes.

### 2.7. Statistical analysis

Analysis was performed using SPSS version 17.0 statistical package for windows (SPSS, Chicago, IL). Continuous variables were expressed as mean $\pm$ S.D. or range, and qualitative data was expressed in percentages. Unpaired $t$ tests for independent samples were used in comparing continuous data between two groups. The association between continuous variables was tested by linear correlation using Pearson's coefficient. All tests were two tailed, confidence intervals were calculated at 95% level and a $p$-value of $<$ 0.05 was considered significant.