

ORIGINAL ARTICLE

Nerve Conduction Abnormalities in Pre-Diabetics and Asymptomatic Diabetics

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Abstract

Aim: To determine the electrophysiological abnormalities in pre-diabetics and/or asymptomatic diabetics and analyse the role of nerve conduction for recognizing distal symmetric polyneuropathy.

Material and Methods: A total of 180 subjects were categorized as: Group A: healthy Subjects (n=60), Group B Pre-diabetics (IFG +IGT, n=60) and Group C: Asymptomatic type 2 diabetics (n=60)

Results: Electrophysiological studies revealed that amplitude of B/L Sural SNAP and tibial CMAP was significantly lower in affected pre-diabetics and asymptomatic diabetics. The presence of significant f wave latency was also noted in both these groups, more among asymptomatic diabetics. The observations on distal latency and nerve conduction velocity of sensory and motor nerves were statistically nonsignificant.

Conclusion: Sensory nerve abnormality was more obvious than motor nerve abnormality in the pre-diabetic subjects. The changes in amplitude of motor nerve abnormality was observed late in course of disease i.e. in asymptomatic diabetic group than pre-diabetics. The amplitude of sensory nerve action potential and F wave latency parameters were the most sensitive measures of peripheral neuropathy in early diabetics in our study.

Introduction

Commonly used concept of diabetic neuropathy is the presence of symptoms and/or signs of peripheral nerve dysfunctions in persons with diabetics/near diabetes after exclusion of other causes.¹ The neuropathy progresses from functional to structural changes in due course of time. The commonly observed neuropathy in diabetics is distal symmetrical polyneuropathy (DPN) and has a prevalence of about 50%.² The presence of neuropathy in diabetics and/or pre-diabetics is associated with considerable morbidity, mortality and diminished quality of life. The peripheral neuropathy is a complication in approximately 50% of patients with diabetes/near diabetes revealing that remaining 50% of patients with peripheral neuropathy may not have symptoms. The axons are affected in a length dependent manner and this centripetal pattern of axonal degeneration is fundamental to the

clinical presentation and investigative tools.³ Timely identification of loss of protective sensations may allow preventive interventions.

Optimal glycaemic control is the only available measure with proven efficacy in preventing progression of peripheral neuropathy, provided measures are instituted at an early stage, least the condition becomes poorly reversible or even irreversible.

The nerve conduction studies are electro-diagnostic tests which are used to evaluate the ability of the electrical conduction of the motor and sensory nerves. Diabetic peripheral neuropathy is associated with changes in both, nerve conduction velocity and amplitude.⁴ Nerve conduction studies are most objective, accurate and reliable for detecting DPN and

most useful tool for evaluating disease progression. In our study we studied electrophysiological changes for evidence of peripheral neuropathy in pre-diabetics, asymptomatic diabetics and healthy controls.

Material and Methods

Study design: cross sectional study

Study duration: 24 months

Sample size and Inclusion criteria: Total 180 cases divided into three groups

Group A- Healthy participants between age 20-70 years of both genders who on clinical evaluation are not suffering from diabetes, any acute or chronic ailments, on any medications which could influence NCS (n=60).

Group B- men and women aged 20-70 years having established diagnosis of prediabetes with or without signs of peripheral neuropathy (n=60)

Group C- men and women aged 20-70 years with asymptomatic type 2 diabetes with or without clinical evidence of neuropathy (n=60).

Exclusion Criteria

- Patients who deny consent to be a part of study.
- Previous diagnosis of any systemic/infective/toxic/genetic/metabolic/inflammatory diseases related to polyneuropathy
- Patients consuming medications (phenytoin, Antiretroviral, Antitubercular) including diuretics and vitamins
- Alcoholic patients
- Patients of chronic Kidney Disease
- Hyperthyroid or Hypothyroid patients

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- Patients of macrocytic hypochromic anaemia
- Skin lesions or swellings that would interfere with NCS
- Patients who were critically ill that they cannot be transferred for performance of nerve conduction study
- Patients Having Malignancy
- Trauma to lower limbs of any kind

Statistical analysis: Statistical analysis was done by using SPSS version 20th. All parameters are expressed in mean \pm SD. For comparison of Quantitative data of three groups, ANOVA was applied, Tukey Post Hoc test was also used for comparison of two groups. For Comparison of Healthy and Pre-diabetics / asymptomatic diabetics subjects unpaired t-test was applied. Chi-square test was also used to check significance association between different groups and outcome of different variables. P-value was checked at 5 % level of significance.

Results

In the present study, we compared changes in NCS parameters in both prediabetes (Group B) and asymptomatic diabetes group (Group C) with healthy controls (Group A). We extended our analysis for Group D comprising Pre + asymptomatic diabetics. The study was undertaken for analyzing distal latency, Amplitude,

velocity and F wave latency in various studied groups as described below in Tables 2-5.

Similarly, the amplitude of motor Tibial nerve is noted significantly abnormal in asymptomatic diabetics (A vs C) and combined pre + asymptomatic diabetics (A vs D). However, the values are insignificant in pre-diabetic group (A vs B) when compared with healthy participants.

In the same table mean values of both sensory and motor amplitude seems within normal range because of "outlier phenomenon" observed in the study.

We found that total number of abnormal nerve conduction rate in pre-diabetic group was 30% (18/60) and in group C was 58.3% (35/60).

Discussion

Diabetic neuropathies are neuropathic disorders that are thought to result from diabetic microvascular injury involving small blood vessels that supply nerves in addition to microvascular condition that culminate in diabetic neuropathy and responsible for significant morbidity and mortality. The diabetic neuropathies are noticed clinically and on electromyographic studies in situations of pre-diabetics, asymptomatic diabetics and diabetic population. Three general types of diabetic neuropathies are described. They include sensory neuropathy

also called peripheral neuropathy, motor neuropathy and autonomic neuropathy. A variety of evidence suggests neuropathy may occur early in diabetes. The neuropathy associated with IGT is clinically similar to early diabetic neuropathy, with preferential injury to small nerve fibers,⁶ resulting in pain and autonomic dysfunction. IGT and diabetic neuropathy patients share abnormal microvascular endothelial dysfunction. These impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) states, have a high risk of conversion to diabetes.⁷ Thus, early intervention and prompt management at pre-diabetic or early stages of diabetes before development of symptoms prevents further complications. Evaluation of neuropathies undertaken in this study by clinical Michigan criteria's for examination and evaluation and by undertaking electrophysiologic measurements which are sensitive, specific and reproducible measures of the presence and severity of peripheral neuropathy, defining quantitative dysfunction. The role of NCS with MNSI in early detection of subclinical neuropathies makes NCS a suitable test for periodic evaluation of diabetic patients.⁸ The neurological parameters studied were nerve conduction velocity (NCV) expressed in meter per sec (m/S), distal latency (DL) expressed in millisecond (ms) and amplitude of Sensory Nerve Action Potential (SNAP) expressed in microvolt (μ V) and compound muscle action potential (CMAP) expressed in millivolt (mV) and F wave latency of tibial nerve. In this study, total number of abnormal nerve conduction rate was 30% (18/60) in pre-diabetic group and 58.3% (35/60) in

Table 1: Subjects of study were enrolled and categorized on the basis of ADA 2014⁵ criteria*

Diagnosis	Fasting plasma glucose	2-hour OGTT	HbA1C
Normal	<100 mg/dl (5.6 mmol/l)	<140 mg/dl (7.8 mmol/l)	<5.7%
Pre-diabetes	100–125 mg/dl (5.6–6.9 mmol/l)	140–199mg/dl (7.8–11.0 mmol/l)	5.7–6.4%
Diabetes	\geq 126 mg/dl (7.0 mmol/l)	\geq 200 mg/dl (11.1 mmol/l)	\geq 6.5%

*The criteria of ADA 2014, has not changed in 2016.

Table 2: Distal latency of Sural nerve (DSL) and Tibial nerve (DML) in group A, B, C and D

Distal latency (milli sec)	Group A (n=60)	Group B (n= 60)	Group C (n= 60)	Group D (n=120)	P - value			
					Group A vs B	Group A vs C	Group B vs C	Group A vs D (t test)
Sural nerve Rt	2.32 \pm 0.72	2.56 \pm 0.67	2.32 \pm 0.88	2.44 \pm 0.79	P=0.204 NS	P=1.000 NS	P=0.204 NS	P=0.329 NS
Sural nerve Lt	2.50 \pm 0.64	2.61 \pm 0.65	2.50 \pm 0.91	2.56 \pm 0.79	P=0.427 NS	P=0.999 NS	P=0.667 NS	P=0.675 NS
Tibial nerve Rt	3.52 \pm 0.95	3.45 \pm 0.92	3.65 \pm 1.02	3.55 \pm 0.97	P=0.204 NS	P=1.000 NS	P=0.204 NS	P=0.839 NS
Tibial nerve Lt	3.49 \pm 1.03	3.50 \pm 1.05	3.61 \pm 1.15	3.56 \pm 1.10	P=1.00 NS	P=0.117 NS	P=0.838 NS	P=0.721 NS

Above table shows that the Distal latency of B/L Sural and Tibial nerve is statistically nonsignificant in all groups when compared with control group.

Table 3: Conduction velocity of Sural and Tibial nerves in group A, B, C and D

Conduction velocity (m/s)	Group A (n=60)	Group B (n= 60)	Group C (n= 60)	Group D (n=120)	P - value			
					Group A vs B	Group A vs C	Group B vs C	Group A vs D (t test)
Sural Nerve Rt	73.54 \pm 20.47	71.68 \pm 23.69	77.76 \pm 24.15	74.72 \pm 24.02	P=0.897 NS	P=0.570 NS	P=0.314 NS	P=0.330 NS
Sural Nerve Lt	76.37 \pm 23.18	74.03 \pm 21.30	76.21 \pm 26.85	75.12 \pm 24.16	P=0.854 NS	P=0.999 NS	P=0.872 NS	P=0.836 NS
Tibial Nerve Rt	64.38 \pm 32.07	70.09 \pm 54.49	63.46 \pm 45.86	66.78 \pm 50.26	P=0.767 NS	P=0.993 NS	P=0.700 NS	P=0.737 NS
Tibial nerve Lt	59.02 \pm 20.93	57.47 \pm 20.65	59.67 \pm 44.83	58.58 \pm 34.83	P=0.959 NS	P=0.912 NS	P=0.920 NS	P=0.926 NS

Above table shows that the NCV of B/L Sural and Tibial nerve is statistically nonsignificant in all groups when compared with control group.

Table 4: Amplitude of sural and tibial nerves in group A, B, C and D

Amplitude of sural (µV) and motor (mV)	Group A (n=60)	Group B (n=60)	Group C (n=60)	Group D (n=120)	P - value			
					Group A vs B	Group A vs C	Group B vs C	Group A vs D (t test)
Sural nerve Rt	14.35±4.81	11.45±5.49	11.71±6.74	11.58±6.13	P=0.017 S	P=0.034 S	P=0.966 NS	P=0.003 S
Sural nerve Lt	14.96±5.86	11.86±5.33	10.79±5.13	11.33±5.24	P=0.006 S	P<0.0001 S	P=0.995 NS	P<0.0001 S
Tibial nerve Rt	15.95±3.92	12.86±4.85	10.91±4.42	11.89±4.72	P=0.235 NS	P<0.001 S	P=0.004 S	P<0.0001 S
Tibial nerve Lt	17.32±5.32	14.06±6.30	11.57±4.72	12.82±5.68	P=0.597 NS	P<0.0001 S	P=0.038 S	P<0.0001 S

Above table shows that the amplitude of sural SNAP is statistically significantly abnormal in pre-diabetic (A vs B) and asymptomatic diabetic (A vs C) and highly significant in combined group (A vs D) when compared with healthy participants on either side. The sensory amplitude values are insignificant with group of pre-diabetic vs asymptomatic diabetes bilaterally (B vs C).

Table 5: Distribution of subjects according to F wave latency in groups

F wave latency	Group A	Group B	Group C	Chi-square value	p-value
Yes	00	12 (20.0%)	19 (31.7%)	21.58	P<0.0001 S
No	60 (100%)	48 (80.0%)	41 (68.3%)		
Total	60 (100%)	60 (100%)	60 (100%)		

Above table shows, out of 60 pre-diabetics 20% i.e. 12 patients had presence of F wave latency and in asymptomatic diabetics it was found in 31.7% i.e. 19 patients, higher than prediabetics. And this observation was found statistically highly significant (P<0.0001) in prediabetics and asymptomatic diabetics compared to healthy controls.

group C. The amplitude of Sural SNAP, Tibial CMAP and f wave latency were found to be most sensitive parameter in detecting peripheral neuropathy in the studied groups. Sensory nerve abnormality was more obvious than motor nerve abnormality in the both groups. The amplitude study of sensory and motor component revealed that the onset of sensory component is earlier in pre-diabetics and marches forward when patient enters zone of asymptomatic diabetes indicating viability of axons damaged. The changes in motor nerve abnormality were noted late in course of disease i.e. in asymptomatic diabetic group. This study did not found any changes in distal latency and nerve conduction velocity of both sensory (Sural) and motor (Tibial) nerves on either side. In present study, the abnormality in f wave latency was found statistically significant (P<0.0001) in both pre-diabetics and asymptomatic and this observation implies that F wave latency is an earlier and vital indicator for peripheral neuropathy where distal motor latency or nerve conduction velocities are not helpful. F-waves of the tibial nerves are the most sensitive measure to detect subclinical or overt diabetic.⁹

Results of this study were comparable to studies conducted by various authors who had reported that DPN usually involve the distal lower extremities with sensory involvement greater than motor and autonomic. Involvement of motor nerves occur later in development of disease.

A study by Yunqian Zhang et al 2014¹⁰ on Amplitude of sensory nerve

action potential in early stage diabetic peripheral neuropathy of 500 cases correlates with our study which has shown the extent of impairment is more in lower extremity than upper and affection of sensory nerve is more than motor nerves. Therefore, nerve conduction especially amplitude of sensory nerve action potential detection, should be routinely examined.

A study by Im Sun et al 2012¹¹ also confirmed that the SNAP amplitude and also tibial CMAP amplitude were significantly smaller in cases of IGT as compared to healthy group. The findings which correlates with the present study.

A study by Soley Thrainsdottir et al 2009¹² found out that there was low sural nerve amplitude and conduction velocity in cases of impaired glucose tolerance as compared to the normal control group. The observation finding of low sural nerve amplitude correlates with the present study. We did not find any abnormality in nerve conduction velocity as described by Soley et al. The reason could be different methodologies adapted in the studies.

A study by Pan H et al 2014⁹ in their study evaluated the sensitivity of electro physiologic assessments and compared F-waves and motor and sensory nerve conduction studies among patients with diabetics. They found that F-waves of the tibial and fibular nerves are the most sensitive measure to detect subclinical or overt diabetics which correlates with the present study.

A study by Sumner CJ et al 2003¹³ in their study found that Patients with

IGT had predominantly small fiber neuropathy, compared to patients with DM, who had more involvement of large nerve fibers. Thus they concluded that neuropathy is associated with IGT though it is milder than the neuropathy associated with DM which correlates with the present study.

Conclusion

The physiological properties of nerve and muscles are modified due to derangements of pathophysiological changes in diabetes mellitus. In our study results conclude that changes of diabetes peripheral neuropathy affected sensory as well motor nerves in both the limbs. Nerve conduction studies are useful aid in diagnosing, monitoring the development of early diabetic peripheral neuropathy when clinical parameters viz. history and clinical examination remains inconclusive. Though clinical examination and history components are essential in evaluation of diabetic peripheral neuropathy, electromyography and nerve conduction study are of paramount importance even in asymptomatic and pre-diabetes. Virtuosity of presence of diabetes mellitus per se is not that important than the presence of diabetic peripheral neuropathy (DPN). The DPN is significantly associated with higher dreaded complications like cerebrovascular stroke and cardiovascular morbidity and mortality. F wave latency measurement and sensory amplitude are of paramount importance especially in asymptomatic and pre-diabetic categories for, motor components abnormalities are observed late in course of the disease, revealed in this study.

References

1. Boulton AJM. Management of Diabetic Peripheral Neuropathy. *Clinical Diabetes* 2005; 23:9-15.
2. Tesfaye S, Selvarajah D. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. *Diabetes Metabolism Research and Reviews* 2012; 28:8-14.
3. Valerie DM, John GM, Barry I, et al. Variability in function measurements of three sensory foot nerves in neuropathic

- patients. *Diab Res Clin Pract* 1995; 29:37-42.
4. Liu MS, Hu BL, Cui LY, et al. Clinical and neurophysiological features of 700 patients with diabetic peripheral neuropathy. *Zhonghua Nei Ke Za Zhi* 2005; 44:173-176.
 5. American Diabetes Association. Diagnostic criteria for diabetes and pre-diabetes. *Diabetes Care* 2014; 37:515-16.
 6. Smith AG, Singleton JR. Impaired glucose tolerance and neuropathy. *Neurologist* 2008; 14:23-29.
 7. Nichols GA, Hillier TA, Brown JB. Progression From Newly Acquired Impaired Fasting Glucose to Type 2 Diabetes: Response to Dinneen and Rizza. *Diabetes Care* 2007; 30:e80.
 8. Fateh HR, Madani SP, Heshmat R, et al. Correlation of Michigan neuropathy screening instrument, United Kingdom screening test and electro diagnosis for early detection of diabetic peripheral neuropathy. *Journal of Diabetes and Metabolic Disorders* 2016; 15:8.
 9. Pan H, Jian F, Lin J, et al. F-wave latencies in patients with diabetes mellitus. *Muscle and Nerve* 2014; 49:804-8.
 10. Zhang Y, Li J, Wang T, et al. Amplitude of sensory nerve action potential in early stage diabetic peripheral neuropathy: an analysis of 500 cases. *Neural Regeneration Res* 2014; 9:1389.
 11. Im S, Kim S-R, Park JH et al. Assessment of the medial dorsal cutaneous, dorsal sural, and medial plantar nerves in impaired glucose tolerance and diabetic patients with normal sural and superficial peroneal nerve responses. *Diabetes Care* 2012; 35:834-839.
 12. Thrainsdottir S. Peripheral polyneuropathy in type 2 diabetes mellitus and impaired glucose tolerance, Correlations between morphology, neurophysiology and clinical findings, Doctoral Dissertations Series, 67, Lund University, Faculty of Medicine, 2009.
 13. Sumner CJ, Sheth S, Griffin JW, et al. The spectrum of neuropathy in diabetes and impaired glucose tolerance. *Neurology* 2003; 60:108-111.