Section: Neurology

Original Research Article

# ELECTROPHYSIOLOGICAL EVALUATION OF SUBCLINICAL NEUROPATHY IN DIABETES PATIENTS

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## Abstract

**Background:** Diabetes mellitus is estimated to affect 23.6 million people in the United States and this number is much larger in India. The risk of developing symptomatic neuropathy in patients without neuropathic symptoms or signs at the time of diagnosis is estimated to be 4 % to 10 % by 5 years and upto 50 % by 25 years. Nerve conduction study is widely used for the diagnosis of diabetic neuropathy. Nerve conduction abnormalities exist in subclinical stages of neuropathy that can be detected at an early asymptomatic stage by various electrodiagnostic test. Because peripheral nerves have the capability to regenerate, early diagnosis and timely intervention will reduce the morbidity in diabetes. **Materials and Methods:** The study is conducted at government Rajaji Hospital, Madurai from April 2021 to April 2022. 30 patients diagnosed as diabetes, who were asymptomatic regarding neuropathy attending the diabetology outpatient department are examined at neurology outpatient department. **Result:** Regarding duration of diabetes, majority of the patients were between 2-5 years (50 %). Among the results compared with each of the CMAP and SNAP, it has been found that as HbA1C level higher, the number of patients showing subclinical nerve conduction abnormality including CMAP median, ulnar, peroneal and tibial nerves shows an increase in patients though not statistically significant. With regarding to HbA1C levels and SNAP, it has been found that SNAP median and sural nerve showed a statistically significant involvement of the nerves as the HbA1C levels raises. **Conclusion:** The present study is done to study the effect of diabetes in motor and sensory nerve conduction parameters in diabetes patients and to observe the functional status of peripheral nerve in asymptomatic diabetes patients. In the present study, almost all patients (26 out of 30 cases) had shown electrophysiological changes indicating that they may had subclinical neuropathy which stresses the importance of the nerve conduction study (NCS) in the diagnosis of subclinical neuropathy. Particularly in sustained hyperglycemia.

## INTRODUCTION

Diabetes mellitus is estimated to affect 23.6 million people in the United States and this number is much larger in India. This trend is largely attributed to the increased prevalence of overweight and obesity. The microvascular complications of diabetes include Retinopathy, Nephropathy and Neuropathy. Patients with sufficient duration of diabetes are vulnerable to the above complications.[1]

Diabetic neuropathy is defined as the presence of symptoms and signs of peripheral nerve dysfunction in diabetes after exclusion of the other causes. Diabetes is the leading cause of peripheral polyneuropathy in developed countries.[2] In general, to define diabetic neuropathy, should be based on symptoms, objective signs and EDX confirmation.

The risk of developing symptomatic neuropathy in patients without neuropathic symptoms or signs at the time of diagnosis is estimated to be 4 % to 10 % by 5 years and upto 50 % by 25 years. Longer duration of diabetes and male sex predispose tot the development of neuropathy over time in type 1 DM. In type 2 DM the risk increased with the duration of the disease. The prevalence of neuropathy is significantly higher among the diabetes who


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consume excessive amounts of alcohol. Tobacco use predispose to early development and more severe symptoms of neuropathy, presumably by inducing vasoconstriction and nerve ischaemia (Bradley text book of neurology 7th edition P.no-1839 1).

Nerve conduction study is widely used for the diagnosis of diabetic neuropathy. Nerve conduction abnormalities exist in subclinical stages of neuropathy that can be detected ata an early asymptomatic stage by various electrodiagnostic test.[3] Because peripheral nerves have the capability to regenerate, ealy diagnosis and timely intervention will reduce the morbidity in diabetes.

This study is used to evaluate the electrophysiological profile in type 2 diabetes patients for the identification of subclinical neuropathy.[4]

**Aim of the study**

1. To study the effect of diabetes in motor and sensory nerve conduction velocity of peripheral nerves in diabetes patients.
2. To observe the functional status of peripheral nerve in asymptomatic diabetes patients

## MATERIALS AND METHODS

The study is conducted at government Rajaji Hospital, Madurai from April 2021 to April 2022. 30 patients diagnosed as diabetes, who were asymptomatic regarding neuropathy attending the diabetology outpatient department are examined at neurology outpatient department.

**Inclusion criteria**

1. Patient diagnosed as diabetes who are asymptomatic regarding neuropathy.
2. Age group of 20 to 60 years. Male and females.

**Exclusion criteria**

1. Diabetes with neuropathic symptoms.
2. Peripheral neuropathy due to other causes – liver, renal dysfunction.
3. Radiculopathy due to cervical spondylosis
4. Hypothyroidism.
5. History of long-term alcohol consumption and prolonged contact with poisonous substance.
6. Age - < 20 and > 60 years.

**Study design**

A detailed medical history, family history and clinical examination was done. Those patients who satisfied the inclusion criteria were selected for further evaluation. Serum fasting blood sugar and post prandial blood sugar is done on the day of nerve conduction study. HbA1C is also done simultaneously. Other blood investigations, blood urea, serum creatinine, liver function test, complete hemogram and thyroid profile is also done.

Nerve conduction studies were performed using standard techniques. Both motor and sensory nerve conduction are done in each patients. Autonomic function testing is not included in this study. Motor NCS is done on both median, ulnar peroneal and tibial nerves. CMAP latency, amplitude and conduction velocity are recorded. The values are compared with the reference value from our laboratory.

## RESULTS

Regarding duration of diabetes, majority of the patients were between 2-5 years (50 %). The next group to follow s < 2 years duration (33.3%) and finally > 5 years duration (16.7%) [Table 1].

**Table 1: Duration of Diabetes**

| Duration of diabetes (yrs) | No of cases | Percentage |
|---|---|---|
| <2 | 10 | 33.3 |
| 2-5 | 15 | 50 |
| >5 | 5 | 16.7 |
| Total | 30 | 100 |

**Table 2: CMAP-Median nerve & Ulnar nerve**

| Nerves | Type | No.of cases | Percentage |
|---|---|---|---|
| CMAP-Median | Normal | 18 | 60 |
| | Axonal | 5 | 16.7 |
| | Demyelinating | 7 | 23.3 |
| CMAP –Median nerve side affected | Normal | 18 | 60 |
| | Left | 5 | 16.7 |
| | Right | 7 | 23.3 |
| CMAP-Ulnar | Normal | 22 | 73.3 |
| | Axonal | 4 | 13.3 |
| | Demyelinating | 2 | 6.7 |
| | Both | 2 | 6.7 |
| CMAP-Ulnar nerve side affected | Normal | 22 | 73.3 |
| | Left | 3 | 10 |
| | Both | 5 | 16.7 |

**Table 3: SNAP median & Ulnar nerve**

| Nerve | Type-side | No of cases | Percentage |
|---|---|---|---|
| SNAP- Median nerve | Normal | 7 | 33.3 |
| | Axonal | 6 | 16.7 |
| | Demyelinating | 7 | 23.3 |
| | Both | 10 | 33.3 |


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| | | | |
|---|---|---|---|
| SNAP-Median nerve affected side | Normal | 7 | 33.3 |
| | Left | 3 | 10 |
| | Both | 20 | 56.7 |
| SNAP-Ulnar neve | Normal | 26 | 86.7 |
| | Axonal | 1 | 3.3 |
| | Demyelinating | 1 | 3.3 |
| | Both | 2 | 67 |
| SNAP-Ulnar nerve side involved | Normal | 26 | 86.7 |
| | Right | 2 | 6.7 |
| | Both | 2 | 6.7 |

**Table 4: Final interpretation**

| Final interpretation | No. of cases | Percentage |
|---|---|---|
| Normal | 4 | 13.3 |
| Both | 26 | 86.7 |
| Total | 30 | 100 |

**Table 5: HbA1C level and CMAP median nerve, Ulnar nerve, Peroneal nerve & tibial nerve**

| Nerve | HbA1C | NORMAL | Abnormal | P value |
|---|---|---|---|---|
| CMAP-Median nerve | < 8 14) | 10 | 4 | 0.759 not significant |
| | >8 16) | 8 | 8 | |
| CMAP-Ulnar nerve | < 8 14) | 11 | 3 | 0.355 not significant |
| | >8 16 | 11 | 5 | |
| CMAP-peroneal | <8 14 | 14 | 0 | 0.919 not significant |
| | >8 16 | 7 | 9 | |
| CMAP-Tibial nerve | <814 | 12 | 2 | 0.609 not significant |
| | >8 16) | 10 | 6 | |

**Table 6: HbA1 and SNAP median, ulnar, sural nerve**

| Nerve | HbA1C | Normal | Abnormal | P value |
|---|---|---|---|---|
| SNAP-Median | <8(14) | 5 | 9 | 0.027 significant |
| | >8 (16) | 2 | 14 | |
| SNAP-Ulnar nerve | <8(14) | 14 | 0 | 0.178 not significant |
| | >8 (16) | 12 | 4 | |
| SNAP Sural nerve | <8(14) | 6 | 8 | 0.027 sigificant |
| | >8 (16) | 2 | 14 | |

Out of 30 cases, 40 % cases showed abnormal Median –CMAP. [Table 2] and showed in [Figure 1].

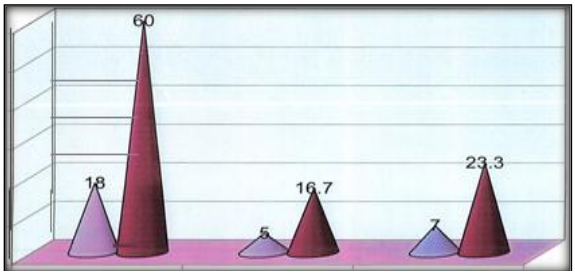


**Figure 1:**

Out of the above abnormal cases, majority of them had involvement of right median nerve (23.3%) [Table 2]. Out of 30 cases,27.7 % cases showed abnormal ulnar CMAP. 13.3 % cases showed axonal [Table 2]. And reported in [Figure 2].

Out of 8 cases showing abnormal CMAP in ulnar nerve, majority of them had involvement on both sides (16.7 %) [Table 2]. Out of 30 cases, nearly 20 cases (66.6%) showed abnormal median nerve SNAP [Table 3]. Out of the affected cases, both sides SNAP median nerve (56.7%) is affected in majority of cases [Table 3]. And showed in [Figure 3].

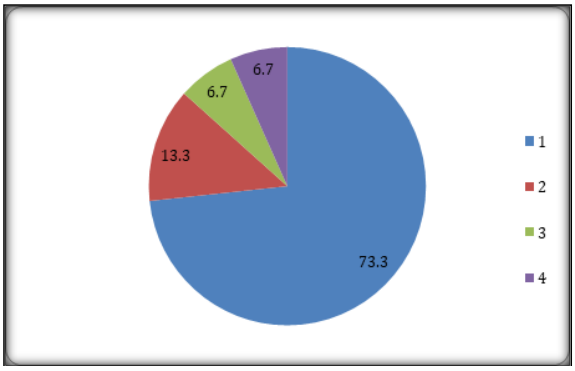


**Figure 2:**

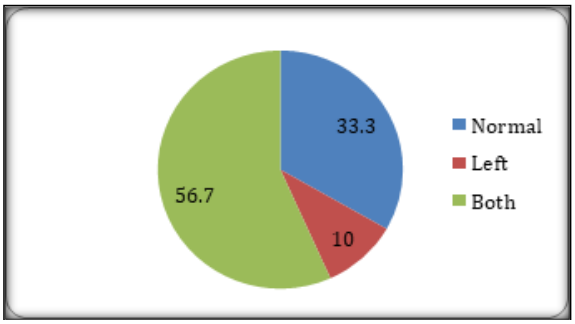


**Figure 3:**

Out of 30 cases, only 4 cases (13.3%) showed abnormal ulnar SNAP [Table 3].


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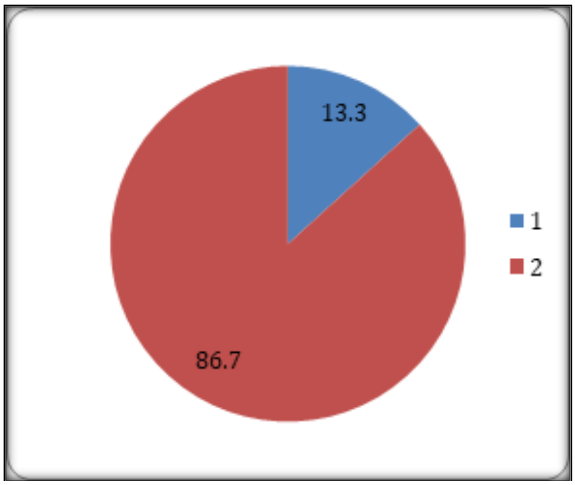


**Figure 4:**

**HbA1C levels and nerve conduction study results:** Based on HbA1C levels, we have divided our population in to two groups –those with HbA1C less than or equal to 8 and those with HbA1C levels more than 8. Among the results compared with each of the CMAP and SNAP, it has been found that as HbA1C level higher, the number of patients showing subclinical nerve conduction abnormality including CMAP median, ulnar, peroneal and tibial nerves shows an increase in patients though not statistically significant [Table 5]. With regarding to HbA1C levels and SNAP, it has been found that SNAP median and sural nerve showed a statistically significant involvement of the nerves as the HbA1C levels raises [Table 5].

## DISCUSSION

Diabetic neuropathy is one of the complications that contribute to the morbidity of such diabetic patients. There are evidence stating that earlier subclinical diabetic neuropathy diagnosis can result in fewer diabetic foot ulcers and amputations,[4] there is also a strong association between polyneuropathy, duration of diabetes and the level of HbA1C, there by indicating that near normal glycemic control should be precautions to delay the beginning or progression of polyneuropathy.[5-8]

An extensive study conducted by Pitrat J.et al,[9] of nearly 4400 clinical patients, reported a prevalence rate of diabetic neuropathy ranging from 7 % of individuals within one year of diagnosis to 50 % for those with diabetes for more than 25 years. The risk for complications of neuropathy increases with increasing duration and severity of hyperglycemia. Hence by estimating both the nerve conduction study and the HbA1C levels, we can identify the risk category for diabetic neuropathy.

The present study is done to study the effect of diabetes in motor and sensory nerve conduction parameters in diabetes patients and to observe the functional status of peripheral nerve in asymptomatic diabetes patients.[10,11]

Out of 30 cases, most of our patients had duration of diabetes being 2-5 years 50 %).Most of the studies done in diabetes had duration over a period of 1-10 years.

Regarding diabetic control in our population it has been found that 16 study had HbA1C level more than 8 53.33 %) and 14 patients had HbA1C level less than 846.6%).

Electrophysiological study was conducted in all the patients. Four of the patients had normal NCS. Out of the remaining 26 cases, majority of the patients had normal sensorimotor polyneuropathy. The next common type of neuropathy noted in our study was predominant sensory neuropathy was noted in three patients. One of the patient had isolated sensory nerve involvement both ulnar sensory, median sensory and sural nerve. The above findings are in concordance with many studies, starting from Abida et al which showed sensorimotor polyneuropathy as the most common type in their group.

Another study done by Balaji et al who studied nerve conduction profile in type 2 diabetes, he concluded that "The most common pattern of neuropathy noted in our study is distal symmetrical sensory and motor polyneuropathy".

Out of the 26patients, with regard to neuropathy pattern in each nerve, axonal pattern predominated in ulnar and peroneal motor study. Demyelinating pattern predominated in median, tibial CMAP and median SNAP. Regarding ulnar nerve involvement, 2 patients had axonal with secondary demyelination pattern, four patients had axonal pattern and two patients had demyelinating pattern.

Sural nerve pattern predominately showed axonal with secondary demyelination pattern.

In our study out of 26 cases, the nerve that are most commonly affected in the decreasing order as follows – median SNAP, sural SNAP, median CMAP, peroneal CMAP, tibial CMAP, ulnar CMAP and ulnar SNAP. Most common nerve affected in upper limb is median nerve, while in lower limb is sural nerve. Thus our study results also correlates with the study done by Anitha varma et al.[6] In which they found that sural and median are commonly affected.

Our study also showed that lower limb nerves are more affected compared to upper limb nerves which is in concordance with the findings of Zahed Ali et al.[7]

In another study conducted by K. Munshiker et al conduction velocity of compound muscle action potential of motor nerves of lower limb – common peroneal nerve and posterior tibial nerve were significantly decreased. The difference in sensory nerve conduction and motor nerve conduction may be due to diameter and myelination of sensory and motor nerve. According to Erlanger and Gasser classification of motor nerve and large diameter nerves and groups under Aa. Most of sensory nerves A and Ao neurons whose diameter are less compare to motor neuron. In Diabetes mellitus sensory nerves are affected first.


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In the present study, almost all patients 26 out of 30 cases had shown electrophysiological changes indicating that they may had subclinical neuropathy which stresses the importance of the nerve conduction study NCS in the diagnosis of subclinical neuropathy. Particularly in sustained hyperglycemia. This result of our study is in accordance with the findings of I.W. Muflih et al study.[9]

In a study conducted by Grat et al,[10] it had been shown that increased glycemic level was associated with abnormal NCV. In our study there is a significant abnormality of nerve conduction study as HbA1C increases, especially with sural SNAP and median SNAP showing that our study is in concordance with the above study. Our study also showed that as HbA1C raises, the pattern of nerve involvement was axonal, especially peroneal and tibial nerves.

Another study done by Saboohi et al,[11] also suggested that HbA1C level exhibit an inverse co relation with NCV of ulnar, tibial nerves in type 2 diabetes aged 40-70 years. In our study the least affected nerve was ulnar nerve.

In a study conducted by Hylienmark.et al,[12] which was a prospective study conducted in type 1 diabetes, it has been concluded that the strongest predictor for the development of a clinical neuropathy was poor metabolic control early on in the disease i.e. up to the baseline examination. HbA1C at follow –up showed a less pronounced correlation with the presence of clinical neuropathy. In our study, which has been done among 30 asymptomatic type 2 diabetes patients, it has been found that higher the HbA1C value, more the nerve involvement, even though statistically not significant and more severe the pathology i.e, axonal type as the HbA1C values are higher. Hence it goes with the above study that poor metabolic control is associated with neuropathy.

In a study conducted by Weisman A et al,[13] it has been concluded that individual NCS parameters or their simple combinations are sufficiently valid measures for identification and future prediction of DSP. It has also been said that sip le combinations of nerve parameters may enhance the detection of incipient nerve injury which is characterized by subtle electrophysiological abnormalities. Our study showed definite involvement of nerve fibers in nearly 26 out of 30 cases, which can predict the future occurrence of diabetic neuropathy.

In a study conducted by Xuan Kong et al,[14] DPN was identified in 52.6 % of patients in another 19.3 % of patients the electrodiagnostic encounter yielded normal results, our study showed evidence of neuropathy in nearly 86.7 % 26 cases and only 13.3% of individual yielded normal results 4 cases).

With regarding to the duration of diabetes and neuropathy. Our study did not show any statistically significant association. This may be probably due to small number of cases 30 cases).

In a study done of by Abida Farheem et al,[8] it has been concluded that nerve conduction velocity progressively decreased from the controls to diabetics with good glucemic control, to the diabetics with poor glycemic control. There is negative correlation between sensory nerve conduction velocity & glycemic control HbA1C In our study, it has been found that as HbA1C level increases, nerve conduction velocity decreases.[15]

On the contrary, DCCT trial and Sosenko et al, found no correlation between HbA1C levels and peripheral neuropathy.[5]

## CONCLUSION

- The results of the present study done in diabetics without complications with duration of diabetes, indicate that there is a significant impairement of mtotr and sensory nerve parameters even though they are asymptomatic.
- We also found a negative correlation between HbA1C levels and nerve conduction parameters Median and sural SNAP. This indicates that poor metabolic control causes early onset and rapid progression of neuropathy.
- We conclude the study with the observation that nerve conduction study can be used as a screening tool to diagnose neuropathy in subclinical stages and should be considered at risk category for aggressive glycemic control by diet, drugs and life style modification to prevent progression of neuropathy.

**Limitation**

The study is done in a small population (thirty cases).

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