ELECTROPHYSIOLOGICAL CHANGES IN PATIENTS OF DIABETES MELLITUS

Ekta Maurya*, B. D. Singh, Shashank Shekhar Sinha*****

*Senior Resident, Department of Physiology,Maharani Laxmi Bai Medical College, Jhansi, **Associate Professor, Department of Physiology,Maharani Laxmi Bai Medical College, Jhansi, ***Associate Professor, Department of Physiology, RDASMC, Ayodhya

Abstracts:**Objective:** Diabetes mellitus (DM) is the third most common cause of morbidity and mortality, after cardiovascular diseases and malignancies[1]. According to recent WHO estimates, the prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030[2]. This study is to evaluate the electrophysiological changes in lower limb in patients of Diabetes mellitus of different duration and correlation with glycemic control.**Method:** A total of one hundred patients of type 1 and type 2 diabetes mellitus were randomly selected from OPD and ward of department of Medicine of MLB Medical College, Jhansi and their Nerve Conduction Study (NCS) of lower limb was performed by physiopac apparatus in department of Physiology, MLB Medical College, Jhansi.**Result:** Diabetic neuropathy has significant correlation with HbA1C and duration of diabetes. Poor glycaemic control and duration of diabetes increases risk of occurrence of peripheral neuropathy, these are important predictors of Diabetic Peripheral Neuropathy.**Conclusion:** Early and immediate interventional measures like good glycaemic control, increase in physical activity, modification in dietary habits, healthy life style and regular surveillance are required to prevent diabetes related neuropathy and other complications.

Key Words: Diabetes Mellitus, Glycosylated haemoglobin, Diabetic Peripheral neuropathy, Nerve conduction study, Common Peroneal nerve, Sural nerve.

Author for correspondence: Dr.Shashank Shekhar Sinha, Department of Physiology, Rajarshi Dashrath Autonomous State Medical College, Ayodhya-224133.e- mail:drshashanksinha@gmail.com

Introduction:

Diabetes mellitus, the most common endocrine disorder is characterized by metabolic abnormalities and in the long run with micro and macro vascular complications that cause significant morbidity and mortality[1]. Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease[2,3]. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India[4,5]. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "Diabetic capital of the world"[6]. Diabetic neuropathies are a disabling complication of diabetes mellitus. India stands at vital place on the earth by contributing most number of diabetics. The mortality rate according to WHO is 26 per 100,000 individuals. In India, the South Indians are more prone to develop diabetes than North Indians. In south India, Hyderabad is at top position with prevalence of 16.6%, followed by Chennai 13.5% and Bangalore 12.4%.Sensori-motor distal symmetric poly neuropathy is the commonest and wide spread form among all neuropathies. Clinical examination of the patient usually reveals absence of pain, temperature, pressure, vibration senses and joint position sense that sequentially place the diabetic foot at ulceration, gangrene and amputation risk.[7,8] The functional ability of any nerve is decided by the conduction velocity, which in turn lies in the hands of inter nodal distance, degree of myelination and nerve diameter.[9] In DPN the nerve undergoes atrophy and Wallerian degeneration that starts in a slowly progressive manner majorly affecting sensory fibers followed by motor fibers.[10,11]

In most patients, the symptoms of polyneuropathy are mild and consist of numbness or paraesthesia of the toes and sensory disturbances often described as like "walking on pebbles" or having "cotton bunched up under the toes". In some patients, "positive" symptoms are present. These include superficial burning, paraesthesia, deep aching pains, dysesthesia, contact induced discomfort and paroxysmal jabbing pains. These symptoms are typically more severe at night. The study was conducted to find out the clinical and electrophysiological pattern of sensori-motor neuropathy in and also to determine whether an association exists between the severity and duration of diabetes and the nerve conduction

patterns of neuropathy. Diabetic neuropathy prevalence was also compared at different duration of diabetes.

Material and Methods:

Present study was carried out in M L B Medical College, Jhansi over a period of 1 year i.e., from February 2019 to January 2020.Prevalence of PN in diabetic patients ranges from around 10.5% to 32.2% in various studies across India. If we take the prevalence of peripheral neuropathy15% and apply the $4pq/l^2$ sample size comes to 204 and approximately taken 200, after getting the consent from100 patients oftype 1 and type 2 diabetes admitted in ward or attendingO.P.D. were included in the study.

Inclusion Criteria:

- All patients of type 1 and type 2 diabetes mellitus of duration 10 years or more, with or without symptoms of diabetic sensori-motor neuropathy.

Diagnostic criteria for diabetes (According to ADA guidelines 2017)

- FPG > 126 mg/dl
- 2 hr PG > 200 mg/dl during on OGTT
- HbA1c > 6.5%
- In patient with classical symptoms of hyperglycaemia or hyperglycaemic crises a random glucose > 200 mg/dl
- If the result are near margin test should be repeated after 3-6 months.

Exclusion Criteria:

- Patients of age more than 60 years.
- Patients with diabetes mellitus with other cause of neuropathy such as alcoholics, smokers, pregnant females, CLD.
- Any pathology or injury to the lower limb.
- Clinical evidence of any other illness like advanced liver disease, autoimmune disease and collagen vascular disease.

Detailed socio-demographic data, family history and medical history was taken from all the subjects and their physical and clinical examinations were done on the very first day of the visit to OPD or ward. A detailed account of the treatment was taken, i.e., whether they are on oral hypoglycemicagents or insulin. Informed consent was taken from each of the subjects.

Each patient was questioned systematically with regard to symptoms of neuropathy and the areas or limbs involved, with special attention to distal symmetric sensorimotor involvement. The duration of diabetes was enquired and confirmed with the reports of the first diagnostic values. Any history pertaining to other conditions that can cause neuropathy were taken like collagen vascular disorders, rheumatoid arthritis, drugs, chemicals etc. and those with a moderate to long term exposure were excluded.

A fullscaleclinical examination, including a detailed neurological examination was done. Special attention was given to those with sensori-motor symptoms, abnormalities in distal muscles like wasting, asymmetry, etc, were looked for. Reflexes were elicited, and the ankle jerk was particularly looked for, and graded as normal, decreasedor absent. Among the sensory system parameters, all modalities of sensations were tested with a view to determining whether there was a glove &stocking pattern of sensory deficit ora dermatomal pattern. Vibration sensation was tested with a 128 Hz tuning fork, on lower limbs.

A complete nerve conduction study (NCS) was done using aEMG EP MARK 2 machine from MEDICAID SYSTEMS, using the standard protocols and settings. Surface electrodes were used with surface stimulators for recording the motor conduction studies while ring electrodes were used as stimulator with surface electrodes for recording of sensory conduction studies. The electrodes used were of three types, i.e. active, reference and ground. The action potential was measured between active and reference electrode and the ground electrode serves as a zero voltage reference point.

As per convention, the right side was tested first and if an abnormality was present then the left side was tested to confirm a symmetrical involvement or to certify a mono-neuropathy.

The temperature of the examination room was about 30°C. Patients were taken to the room, rested for a while so as to decrease the ambulant temperature to the recommended level of 30-32°C and then the procedure was carried out.

Motor conduction studies were done on common peroneal nerve with respect to latency, amplitude, velocity. Sensory conduction studies were done on sural nerves with respect to latency, amplitude and velocity.

For latency, the distance / time interval was measured from the onset of the action potential curve to the first negative deflection. For sensory studies, the interval between the onset and the first dip in the action potential curve was recorded as well. The amplitudes were measured from the baseline to the peak of the negative deflection. The lengths of the nerves were measured between the 2 stimulation points, proximal and distal. For sensory studies the length was measured from the stimulatory electrode to the receiving electrode locations. The conduction velocity was calculated by dividing the distance (m) by the time (sec) and reading m/sec. These results were also compared with the standard reference values. A deviation of > 2 was considered abnormal.

Observers' variability was reduced to almost nil, as the study was conducted by the same staff for all the patients. The same specialist evaluated and commented on the results.

All the data collected was entered in Microsoft excel and data analysis done in SPSS 20.0 version and appropriate statistical tests were applied.

Result:

This study was conducted to know the electrophysiological and clinical profile of diabetic peripheral neuropathy. Another aim was to determine whether any association existed between duration and status of glycemic control and severity of neuropathy to the electrophysiological profile. In our study out of 200 patients was found as 10% in type 1 diabetes and 90% in type 2 diabetes (Table 1).

Table no. 1: Distribution of cases according to type of diabetes

Type of diabetes	No. of cases	Percentage	Prevalence
Type I	20	10.0	0.1
Type II	180	90.0	0.9
Total	200	100	

The study consists of 200 patients in which 116 were male (58%) and 84 were females (42%). The minimum age was 26 years and the maximum age observed was 85 years and the mean ± SD years.

In our study, among the 200 cases of diabetics, 126 (63%) showed normal NCS report while 74 (37%) showed abnormal NCS reports (Table 2).

Table No. 2: Nerve Conduction Study report

Report of NCS	Number of cases	Percentage(%)
Normal	126	63.0
Abnormal	74	37.0
Total	200	100

In our study it was found that there is strong association between the HbA_1c levels and NCS reports (p = 0.001) and the clinical presentation of neuropathy. HbA_1c levels of < 7 had 12.5%, 7- 8 had 5.5%, 8-9 had 9.5% and >9 had 71% of patients with abnormal NCS reports (Table 3).

Table No. 3: Association of NCS toHbA1C

Hb A_1C (%)	Total no of patients	Normal NCS	Abnormal NCS	Percentage
< 7	32	28	4	12.5
7-8	36	34	2	5.5
8-9	42	38	4	9.5
> 9	90	26	64	71

Chi-square value=82.038,p=0.00001

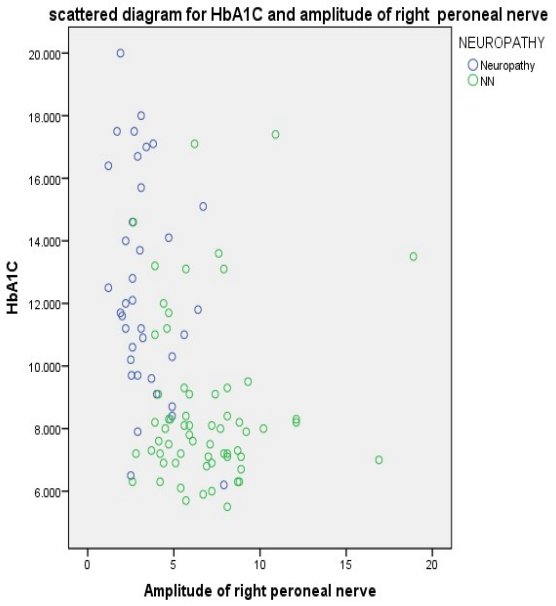
Out of 200 patients 46 patients presents abnormal NCS with duration more than 10 years and only 28

presents with abnormal NCS with duration less than 10 years. So there is strong association between abnormal NCS with increasing duration of diabetes (Table 4).

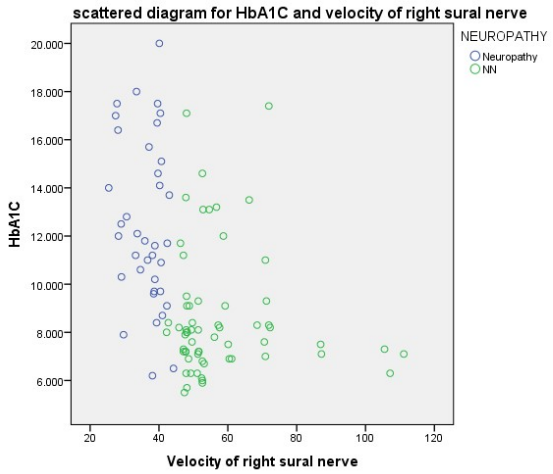
Table no 4: Association between NCS to duration of diabetes.

Duration (yrs)	No of cases	Normal NCS	Abnormal NCS	Percentage
0 - 5	54 (7.5%)	52	4	7.5
5 -10	72(33%)	50	24	33
>10	74(62%)	24	26	62

Chi-square value=19.4 p=0.00006



Following scattered diagram showing frequency of distribution of values of amplitude of common peroneal nerve and HbA1c. More cases of low amplitude values are with high HbA1c and neuropathic cases are more in high HbA1c.



Following scattered diagram frequency of nerve conduction velocity and HbA1c. Decrease conduction velocity more with poor glycaemic control. And neuropathy of sural nerve is more in poor glycaemic control.

Discussion:

In our study it was found that there is strong association between the HbA_1c levels and NCS reports (p=0.001) and the clinical presentation of neuropathy. HbA_1c levels of < 7 had 12.5%, 7- 8 had 5.5%, 8-9 had 9.5% and >9 had 71% of patients with abnormal NCS reports. A study on the Utility of Nerve Conduction Studies in Type 2 Diabetes Mellitus by Shekherappa KR et al[3], found similar result.

Another study by Bansal et al.[4] found that for each 1% increment in HbA1c is associated with an approximately 10–15% increase in diabetic neuropathy frequency. Similar result found in study from China by (Su et al.[5]) has also demonstrated that increased HbA1c variability adds to poor chronic glycaemic control and is closely associated with diabetic neuropathy in patients with type 2 diabetes. Another study supporting our result on Nerve conduction abnormalities in patients with newly diagnosed diabetes mellitus, Aditya Prakash Kulkarni et al[6] found that there was negative correlation with median motor conduction velocity, common peroneal distal motor amplitude, median sensory amplitude, superficial peroneal amplitude, and the sural nerve amplitude with increasing age of the patients ($P < 0.05$). Patients with higher HbA1c had prolonged distal motor latencies and reduced conduction velocities in the upper and lower limbs

with reduction of CMAP amplitude in the ulnar nerve. Median nerve sensory amplitude and velocity were lower in patients with higher HbA1c ($P < 0.05$).

A study done by de Souza *et al*.[12] reported slowing of motor conduction velocity and reduction in amplitude of SNAP to be the earliest evidence of diabetic neuropathy in asymptomatic patients. This is followed by prolongation of sensory latencies, reduction of sensory velocity, and later by reduction in amplitudes of CMAP when patients are likely to manifest clinically.

Another study on evaluation of different HbA1c levels to assess the risk of peripheral neuropathy among Type 2 Diabetic patients along with other conventional risk factors done by Hoque S et al[13]found similar result. Similar result found in studies[14-16] which match with our findings which show significant increase in HbA1C which has effect on NCV in diabetics compared to non-diabetics. This indicated that axonal degeneration and re- innervation process of Neuro muscular junction in diabetic neuropathy are consistent with the metabolic control of this disease.

Similar result found in study by Huang et al[17] observed that the deterioration in nerve conduction velocity was marked in patients with a mean HbA1c of more than 8.5%.

Similar studies[18, 19] find out that HbA1C variability is strongly associated with composite scores of nerve conduction, which are indicative of the degree of severity of DSPN, in patients with type 2 diabetes and the severity of DSPN, expressed by the sum of nerve conduction velocities and distal amplitude scores, was significantly related to glycaemic control

In our study it was also found that there is significant association between duration of diabetes and clinical presentation of neuropathy (p=0.001). Prevalence of symptoms increased with increased duration of diabetes. In our study 28% patients had diabetes for less than 5 years, 37% had diabetes of 5-10 years duration, while 35% had diabetes of> 10 years duration, were found to have a significant association between duration of diabetes and the NCS reports. Diabetic duration of < 5 year had 7.5 %, 5-10 years had 33% and >10 years had 62% of patients with abnormal NCS reports.

Similar result found in study done by S Ashok et al[20]on *Prevalence of neuropathy in type 2 diabetic patients attending a diabetes centre in South India.* Overall, 19.1% of the patients had evidence of neuropathy. The prevalence of neuropathy increased with increase in age ($p < 0.001$) and duration of diabetes ($p < 0.001$). Multiple logistic regression analysis revealed age ($p < 0.001$) and duration of diabetes ($p = 0.001$) as the risk factors for neuropathy.

Conclusion:

In conclusion among the patients studied, diabetic neuropathy has significant correlation with HbA1C and duration of diabetes. Poor glycaemic control and duration of diabetes increases risk of occurrence of peripheral neuropathy, these are important predictors of DPN.Early and immediate interventional measures like good glycaemic control, increases in physical activity, modification in dietary habits, healthy life style and regular surveillance are required to prevent diabetes related neuropathy and other complications.

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