

## ORIGINAL ARTICLES

# Nerve Conduction Study of Newly Diagnosed Type 2 Diabetic Patients and Its Correlation with Glycosylated Hemoglobin (HbA1c)

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### Abstract

**Background:** Peripheral neuropathy is one of the common complications of DM may proceed by a long period of clinically silent impaired glucose tolerance, altering the nerve function by the time diabetes is diagnosed. Nerve conduction study (NCS) remains the most reliable, accurate and sensitive measure for diagnosis of peripheral neuropathy.

**Objectives:** Evaluation of nerve conduction study of newly diagnosed type -2 diabetic patients either and to find out its correlation with glycosylated hemoglobin (HbA1c).

**Method:** This case control study, 50 newly diagnosed type-2 diabetic patients within 1 month of both sex and rest 50 healthy controls were studied during 2018-2020 from outpatient department of Endocrinology and advised to attend the department of Neurology of Dhaka medical college hospital. Nerve conduction study of cross limbs was performed. Blood sugar and glycosylated hemoglobin (HbA1C) were determined.

**Results:** Motor nerve conduction parameters are more affected. Median nerve impairment in both motor and sensory nerve conduction study was statistically significant ( $p<0.05$ ) between case and control group. Most abnormal parameter is CMAP of peroneal nerve 42% followed by DL of tibial (20%) and median(18%) in motor nerve conduction study whose majority of them HbA1C was  $>10\%$ . Combined tibial and peroneal nerve involvements were more common 11 (22.0%). In multivariate regression analysis, HbA1C significantly ( $p<0.05$ ) associated with tibial F-Lat but others were not significantly associated. There were significant positive correlation with median DL ( $r=0.829$ ;  $p=0.002$ ), median F-Lat ( $r=0.814$ ;  $p=0.001$ ), Tibial DL ( $r=0.805$ ;  $p=0.004$ ), tibial F-Lat ( $r=0.832$ ;  $p=0.001$ ), median sensory DL ( $r=0.824$ ;  $p=0.002$ ) **Conclusion:** Increased HbA1c level indicative of a state of hyperglycemia is a risk factor for polyneuropathy in diabetic patients. NCS parameters are valuable for identification, future prediction of diabetic neuropathy as well as quantitative measure of its severity.

**Keywords:** Diabetes Mellitus, HbA1c, Nerve Conduction Study.

### Introduction

Diabetes mellitus is one of the most common chronic diseases globally. It was estimated that in 2017 there were 451 million (age 18–99 years) people with diabetes worldwide who are expected

to increase to 693 million by 2045. The high prevalence of diabetes has important social, financial and development implications especially in low and middle - income countries<sup>1</sup>. Diabetic neuropathy (DN) is one of the most commonly

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occurring microvascular complications accounting for 28% of all the complications in diabetics<sup>2</sup>. Prevalence of diabetic peripheral neuropathy in bangladesh was 19.7% in male and 18.7% in female which increased with age and duration of diabetes<sup>3,4</sup>. Diabetic peripheral neuropathy affecting approximately 8% of newly diagnosed patients and >50% of patients with long-term DM<sup>5</sup>.

It is a progressive process that has a long asymptomatic stage<sup>6</sup>. Approximately 15% of patients with DM develop foot ulcer during their lifetime, of which 70% have a neuropathic origin<sup>7</sup>. The signs, symptoms, and neurologic deficits in DN vary depending on the classes of nerve fibers involved. Diabetic sensorimotor polyneuropathy is the most common clinical subtype seen in clinical practice<sup>8</sup>. Common symptoms are symmetrical paresthesia and burning pain that predominantly occurs distally in the legs according to length dependency<sup>9</sup>. 15% of patients with NIDDM have both symptoms and signs of neuropathy but nearly 50 percent have either neuropathic symptoms or slowing of Nerve Conduction Velocity, before patient develops any sign<sup>10</sup>. Peripheral neuropathy is the frequent, globally disabling and earliest complication among major three complications of diabetes mellitus. Its prevention and early detection is of utmost importance. However, because not all sensory and motor symptoms in the extremities correspond to an electrophysiological abnormality, screening for diabetic peripheral neuropathy in DM patients poses a challenge. Patient with recently diagnosed or poorly controlled diabetes frequently show reduced nerve conduction velocity that improves rapidly with establishment of euglycaemia<sup>11</sup>. Therefore, a quantified, reliable screening tool is required for early detection of diabetic peripheral polyneuropathy.

Nerve conduction studies (NCS) are considered to be the most sensitive, reliable, non-invasive, and objective means of investigating diabetic neuropathy. Routine NCS include evaluation of motor function of the median, ulnar, peroneal and tibial nerves, and sensory function of median, ulnar and sural nerves in terms of onset latency, amplitude, and conduction velocity. F waves are motor responses produced by antidromic activation

of motor neurons following stimulation of motor axons peripherally. Various F-wave parameters such as minimal F-wave latency and persistence have been reported to have a very high diagnostic reliability in diabetic patients. Plasma glycosylated hemoglobin (HbA1C) is an index of average glycemic control over the previous 2–3 months and indicates poor diabetic control; furthermore, increased HbA1C concentration is the most important risk factor for predicting DM complications. Maintaining an HbA1C level below 6.5% is critical to decreasing the incidence of diabetic complications<sup>5</sup>. The HbA1C level could be a screening tool for early detection of diabetic peripheral polyneuropathy and an indicator of the optimal time for performing NCS in patients with long-standing diabetes. Moreover, the quantified composite score of NCS may be associated with disease severity<sup>13</sup>.

Many investigators have studied the correlation between DM complications and HbA1C. However, very little research has considered the correlation between NCS parameters, HbA1C. The objectives of the present study were to evaluate various nerve conduction parameters in newly diagnosed (type 2) diabetic patients and any correlation with HbA1C.

#### **Materials and methods:**

This case-control study was conducted in the department of Neurology, Dhaka medical college hospital, from July 2018 to June 2020 after obtaining ethical clearance. The study sample consisted of newly diagnosed type 2 diabetic patients within 1 month of the diagnosis of as per criteria laid down by American Diabetes Association criteria<sup>14</sup>. The cases were both sexes, aged: ≥18 years attending outdoor department of endocrinology advised to attend in department of neurology. The control group comprises an equal number of age-matched non diabetic healthy individuals. Written informed consent was obtained from all the participants. The patients type 1 DM, chronic diseases such as chronic renal failure, hypothyroidism, hepatic dysfunction, inflammatory neuropathy, vasculitis, CVD, family history of neuropathy, chronic smokers, history of chronic alcohol abuse, toxin, metals or drugs were

excluded. All patients underwent detailed neurological examination and their BMI was calculated.

Neurophysiological examination includes measurement of nerve conduction study of cross limbs. Motor NCS and elicitation of F-waves were performed on median, ulnar, common peroneal and tibial nerves. Sensory conduction study was performed on median, ulnar and sural nerves. With the help of stimulating electrodes supramaximal stimulation was given at two different sites (distal and proximal site) to obtain compound muscle action potential. Ground electrode was placed between stimulating electrode and recording electrode. Nerve conduction velocity was measured by a standard NCV-EMG machine (NIHON KOHDEN), model – MEB9400, software- NeuropackS1 in a room temperature. Nerve conduction parameter included according to the protocol recommended by Antonio Conference on Diabetic neuropathy. Nerves were stimulated using 1 ms electrical pulse at a repetition rate of 1 per second with intensity sufficient to elicit maximum amplitude of compound muscle action potential (CMAP) and sensory nerve conduction potential (SNAP). Nerve function was considered abnormal if any parameter [distal latency, compound muscle action potential (CMAP), sensory nerve action potential (SNAP), conduction velocity (CV) of four motor and three sensory nerve modalities assessed was not the limits of normality.

Data was processed and analyzed using SPSS (Statistical Package for Social Sciences). To

observe the difference between the case and control test statistics like Chi-square ( $\chi^2$ ) was done to compare the qualitative variables and independent t-Test for quantitative variables. To measure the outcome between the case and control, multivariate logistic regression was done for qualitative variables. To observe the correlation HbA1C between the nerve conduction parameters of the patients, scatter diagram was formulated for quantitative variables and linear logistic regression test for the qualitative variables. P value less than 0.05 was considered statistically significant.

#### Results and observations:

Out of total 100 patients, 50 consecutive newly diagnosed type-2 diabetic patients (group 1) 28 (56%) males and 22(44%) females. Mean age was  $45.62 \pm 11.92$  years ranged from 25 to 79 years. Age, sex, religion, occupation, educational status, socioeconomic status in diabetic patients did not differ significantly (P value  $<0.05$ ) with control group (group II). Table 1 shows the mean value of HbA1C level was significantly higher in diabetic group was  $9.23 \pm 2.57$  (%) in group I and  $5.63 \pm 0.61$  (%) in group II (P value was  $<.001$ ).

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On comparison of motor nerve conduction parameters between two groups revealed in table II. P value reached from unpaired t-test. The mean distal latency, compound muscle action potential,

**Table-I**  
*Distribution of the study patients by LAB test (n=100)*

LAB test	Group I(n=50)		Group II(n=50)		P value
	Mean $\pm$ SD	Range (min,max)	Mean $\pm$ SD	Range (min,max)	
Fasting Blood Glucose (mmol/L)	$10.81 \pm 4.84$	5.08,27.61	$4.6 \pm 0.8$	3.3,6.1	0.001 <sup>s</sup>
2 Hours after 75g Glucose drink (mmol/L)	$15.57 \pm 5.3$	8.03,31.86	$5.65 \pm 1.29$	3.3,7.8	0.001 <sup>s</sup>
HbA1C (%)	$9.23 \pm 2.57$	5.04,13.6	$5.63 \pm 0.61$	4.4,6.6	0.001 <sup>s</sup>

conduction velocity, F-Latency of median nerve between cases and controls were significantly deferent( $P<0.05$ ).The mean values are  $3.75\pm0.87$ (ms), $9.0\pm3.63$ (mv)  $45.15\pm6.51$ (m/s)  $29.61\pm1.75$ (ms) respectively for diabetic group &  $3.47\pm0.39$  (ms),  $10.39\pm3.12$  (mv),  $56.02\pm7.19$  (ms),  $26.53\pm2.41$ (ms) respectively for control group. The compound muscle action potential was  $7.75\pm1.92$  in group I and  $9.29\pm2.07$  in group II differ significantly ( $P<0.05$ ).There were no significant difference in mean value of DL, MNCV, F-latency of ulnar nerve. The mean value of distal latency and F-latency for studied tibial nerve was significant difference ( $P<.035,.013$  respectively), whereas mean value of CMAP, MNCV of tibial nerve was not significant different from control group. The

mean value of CMAP of peroneal nerve  $3.45\pm1.63$  in diabetic group &  $4.18\pm1.72$  in control group was differ significantly ( $P<.032$ ). DL, MNCV were comparable but not significant between two groups. While comparison of sensory nerve conduction parameters in diabetic and control group in table III. There was significant difference in mean value of distal sensory latency, SNAP, SNCV for studied median nerve the values were  $2.97\pm0.47$ ,  $28.53\pm16.96$ ,  $45.16\pm7.34$  respectively in diabetic group and  $2.73\pm0.4$ ,  $35.2\pm11.55$ ,  $48.7\pm3.68$  in control group respectively. The mean value of SNCV of ulnar nerve was differ significantly from diabetic to control group ( $P<0.028$ ) .The mean value of SNAP of sural nerve was significantly differ from control group ( $P<0.043$ ).

**Table-II**  
*Distribution of the study patients by motor nerve conduction study (n=100)*

Motor nerve conduction study	Group I(n=50)	Group II(n=50)	P value
	Mean±SD	Mean±SD	
<b>Median nerve</b>			
DL (ms)	$3.75\pm0.87$	$3.47\pm0.39$	0.041 <sup>s</sup>
CMAP (mV)	$9.0\pm3.63$	$10.39\pm3.12$	0.042 <sup>s</sup>
CV (m/s)	$45.15\pm6.51$	$56.02\pm7.19$	0.001 <sup>s</sup>
F-Lat (ms)	$29.61\pm1.75$	$26.53\pm2.41$	0.001 <sup>s</sup>
<b>Ulnar nerve</b>			
DL (ms)	$2.61\pm0.45$	$2.5\pm0.34$	0.171 <sup>ns</sup>
CMAP (mV)	$7.75\pm1.92$	$9.29\pm2.07$	0.001 <sup>s</sup>
CV (m/s)	$57.39\pm6.06$	$55.4\pm6.85$	0.127 <sup>ns</sup>
F-Lat (ms)	$26.47\pm2.65$	$25.8\pm2.38$	0.186 <sup>ns</sup>
<b>Tibial nerve</b>			
DL (ms)	$4.99\pm1.22$	$4.52\pm0.96$	0.035 <sup>s</sup>
CMAP (mV)	$10.48\pm4.09$	$9.19\pm3.29$	0.085 <sup>ns</sup>
CV (m/s)	$44.05\pm5.59$	$45.36\pm13.24$	0.521 <sup>ns</sup>
F-Lat (ms)	$47\pm4.26$	$45.12\pm3.12$	0.013 <sup>s</sup>
<b>Peroneal nerve</b>			
DL (ms)	$3.88\pm0.71$	$3.65\pm0.49$	0.062 <sup>ns</sup>
CMAP (mV)	$3.45\pm1.63$	$4.18\pm1.72$	0.032 <sup>s</sup>
CV (m/s)	$45.39\pm8.59$	$45.62\pm5.46$	0.873 <sup>ns</sup>

**Table-III**  
*Distribution of the study patients by sensory nerve conduction (n=100)*

Sensory nerve conduction	Group I(n=50) Mean±SD	Group II(n=50) Mean±SD	P value
<b>Median nerve</b>			
DL (ms)	2.97±0.47	2.73±0.4	0.007 <sup>s</sup>
SNAP (mV)	28.53±16.96	35.2±11.55	0.024 <sup>s</sup>
CV (m/s)	45.16±7.34	48.7±3.68	0.003 <sup>s</sup>
<b>Ulnar nerve</b>			
DL (ms)	2.25±0.37	2.32±0.33	0.321 <sup>ns</sup>
SNAP (mV)	36.03±16.15	32.5±15.28	0.264 <sup>ns</sup>
CV (m/s)	46.94±6.02	49.88±7.59	0.028 <sup>s</sup>
<b>Sural nerve</b>			
DL (ms)	2.22±0.36	2.24±0.33	0.772 <sup>ns</sup>
SNAP (mV)	17.88±10.06	14.34±6.94	0.043 <sup>s</sup>
CV (m/s)	47.61±7.31	47.67±1.33	0.955 <sup>ns</sup>

For median nerve most frequent abnormal parameters were distal latency( DL) and compound muscle action potential CMAP(21%) whose majority of patients HbA1C was >10%.For ulnar nerve,most frequent abnormal parameter was CMAP(28%) whose majority HbA1C >8%.For tibial nerve,DL(30%)whose majority of patients HbA1C was 6.5-8%. For peroneal nerve,most frequent abnormal parameter was CMAP (57%)whose majority HbA1C was >8% (Table IV).

**Table-IV**  
*Abnormal findings of motor nerve conduction study subjects (n=50)with different level of HbA1C*

Motor nerve conduction study	6.5-8 % (n=20)		>8-10 % (n=7)		>10 % (n=23)	
	n	%	n	%	n	%
<b>Median nerve</b>						
DL ( $\geq 4.4$ ms)	4	20.0	0	0.0	5	21.7
CMAP ( $\geq 4.0$ mV)	1	5.0	0	0.0	2	8.7
CV ( $<30$ m/s)	0	0.0	0	0.0	0	0.0
F-Lat ( $\geq 31$ ms)	1	5.0	0	0.0	0	0.0
<b>Ulnar nerve</b>						
DL ( $\geq 3.5$ ms)	2	10.0	0	0.0	0	0.0
CMAP ( $\geq 6.0$ mV)	2	10.0	2	28.6	5	21.7
CV (m/s)	0	0.0	0	0.0	0	0.0
F-Lat ( $\geq 32$ ms)	1	5.0	0	0.0	0	0.0
<b>Tibial nerve</b>						
DL ( $\geq 6.0$ ms)	6	30.0	0	0.0	4	17.4
CMAP ( $\leq 4.0$ mV)	1	5.0	0	0.0	0	0.0
CV (m/s)	0	0.0	0	0.0	0	0.0
F-Lat ( $\geq 56$ ms)	1	5.0	0	0.0	0	0.0
<b>Peroneal nerve</b>						
DL ( $\geq 5.5$ ms)	0	0.0	1	14.3	0	0.0
CMAP ( $\leq 3.0$ mV)	9	45.0	4	57.1	8	34.8
CV (m/s)	1	5.0	0	0.0	0	0.0

For median sensory nerve, most frequent abnormal parameter were DL and SNAP whose majority HbA1C was 6.5- 8% &>10%. For ulnar nerve, most frequent abnormal parameter was SNAP whose majority HbA1C was 6.5-8%. For sural nerve, SNAP is mostly affected, whose HbA1C was 6.5-8%. Conduction abnormality was not found in the present study except peroneal nerve in motor conduction study (Table V).

Combination nerve involvement with various parameter are Tibial + peroneal (22%) tibial+peroneal+sural(6%), isolated median nerve involvement(12%).

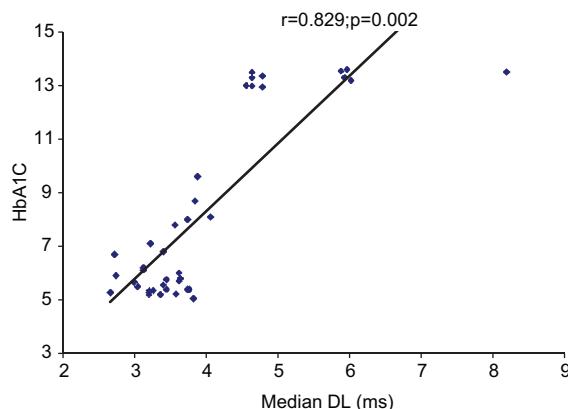
Multivariate regression analysis showed there were no association between HbA1C and different nerve conduction parameters except tibial F-latency ( $P<0.05$ ).

Observations of correlation between HbA1C between different parameters of NCS revealed, there were highly significant positive correlation ( $P<0.05$ ) found in DL and F-latency of median nerve, DL and F-latency of tibial nerve, sensory DL of median nerve. Amplitude and conduction velocity showed inverse but nonsignificant correlation.

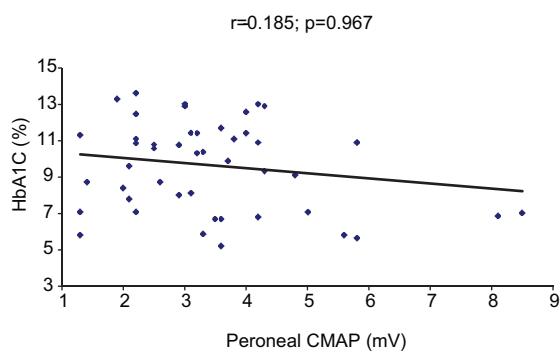
**Table-V**

*Abnormal findings of sensory nerve conduction study subjects (n=50) in different level of HbA1C*

Sensory nerve conduction	6.5-8 % (n=10)		>8-10 % (n=7)		>10 % (n=23)	
	n	%	n	%	n	%
<b>Median nerve</b>						
DL ( $\geq 3.3$ ms)	4	20.0	1	14.3	3	13.0
SNAP ( $\geq 20$ mV)	6	30.0	1	14.3	7	30.4
CV ( $< 30$ m/s)	0	0.0	0	0.0	0	0.0
<b>Ulnar nerve</b>						
DL ( $\geq 3.1$ ms)	0	0.0	0	0.0	2	8.7
SNAP ( $\geq 17$ mV)	3	15.0	1	14.3	3	13.0
CV ( $< 30$ m/s)	0	0.0	0	0.0	0	0.0
<b>Sural nerve</b>						
DL ( $\geq 4.5$ ms)	0	0.0	0	0.0	0	0.0
SNAP ( $\geq 6.0$ mV)	1	5.0	0	0.0	1	4.3
CV ( $< 30$ m/s)	0	0.0	0	0.0	0	0.0



**Fig.-1:** Scatter diagram showing significant positive correlation ( $r=0.829; p=0.002$ ) between the HbA1C and median DL



**Fig.-2:** Scatter diagram showing not significant negative correlation ( $r=-0.185; p=0.967$ ) between the HbA1C and peroneal CMAP

### **Discussion:**

The present study revealed abnormalities in the nerve conduction parameters in patients with newly diagnosed type 2 diabetic patients which correlated HbA1C values. Electrophysiological incidence of peripheral neuropathy was generally found in about 30%. In this study longer latency, smaller amplitude, declining velocity were found in median nerve both motor and sensory conduction study. F-wave latency was also prolonged<sup>8</sup>. The present studies also revealed ulnar prolonged conduction velocity and reduced amplitude, prolonged distal latency and F-latency of tibial nerve, reduced amplitude of peroneal nerve in motor conduction study whereas reduced conduction velocity in ulnar nerve and amplitude in sural nerve<sup>15</sup>. Kulkarni et al. found longer latency, smaller amplitude and slower conduction velocity were found in all nerves and these parameters were inferior in those with higher HbA1C<sup>16</sup>.

In this study, motor nerve conductions were more affected than sensory nerves conduction. Sultana et al. found thirteen patients (54%) had abnormal sensory conductions and nine patients had abnormal motor conductions<sup>17</sup>. They also found significant motor function deterioration in the diabetic groups with shorter and longer duration comparison to healthy group<sup>17</sup>. This finding is consistent with this study. Peroneal nerve was most affected followed by tibial, median motor and sensory, ulnar, sural in descending order<sup>18</sup>. Dyck and O'Brien found peroneal motor nerve had highest abnormality<sup>18</sup>. Singh et al. found that most of the study subjects showed two to five nerve combination, also high percentage of subjects with altered median nerve conduction that correspond to this study<sup>19</sup>. In the correlation observation of this study there was positive correlation with distal latency, F-latency of median and tibial nerve. Other studies also found inverse correlation with conduction velocity<sup>20,21</sup>. Agarwal et al. showed a weak to moderate statistical significant relationship with HbA1C<sup>15</sup>. Smaller amplitude reflects axonal loss and slowing of conduction velocity could be the result of combination of segmental demyelination, loss of fastest conducting axons. Conduction abnormalities are more frequent in

large myelinated fibers in early stage of diabetes but also involvement of small myelinated and unmyelinated fibres especially in lower extremity. Thus nerve length might be an important factor in early dysfunction of nerve<sup>19</sup>.

### **Conclusion:**

The present study showed that abnormalities of NCS parameters in early stage of diabetes at time of diagnosis, thus it is important to evaluate all newly detected diabetics for subclinical impairment of nerve function and incorporation of electrophysiological study as routine test. Occurrence of electrophysiological changes in nerve function correlates with HbA1C.

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