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Motor and Sensory nerve conduction study in patients of Type 2 Diabetes Mellitus

KEYWORDS: Diabetes Mellitus, Diabetic Neuropathy, Nerve Conduction Study.

Dr. Piyali Debbarma
Post graduate student, Department of Physiology, Mahatma Gandhi institute of Medical Sciences, Sewagram, Wardha, Maharashtra

Dr. Nishant Bansod
Associate Professor, Department of Physiology, Mahatma Gandhi institute of Medical Sciences, Sewagram, Wardha, Maharashtra

Dr. Ajay R. Chaudhari
Professor and Head of the Department, Department of Physiology, Mahatma Gandhi institute of Medical Sciences, Sewagram, Wardha, Maharashtra

ABSTRACT : Diabetes mellitus is a common metabolic disorder of multiple aetiology. It may causes neuropathy. Nerve conduction study widely used for the assessment of neuropathies. Hence the aim of present study was to study the motor and sensory nerve conduction parameters in type 2 diabetic patients and control group and compared with themselves. 50 type 2 diabetic patients as cases and 50 normal healthy subjects as controls were enrolled in our study. Motor nerve conduction study which includes distal motor latency, amplitude of compound muscle action potential (CMAP) and conduction velocity in median, ulnar, peroneal and tibial nerves and sensory nerve conduction study which include amplitude of sensory nerve action potential (SNAP) and conduction velocity in median, ulnar and sural nerves were measured. In our study involvement of both motor and sensory nerve conduction parameters were observed.

Introduction:

The term diabetes mellitus describes a "metabolic disorder of multiple aetiology characterised by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both".[1]Generally diabetes can be of two types- Type 1 and Type 2 which accounts for 5-10% and 90-95% respectively.[2,3]

Over the past decade the prevalence of DM has risen dramatically in the worldwide. It is estimated that 171million people had diabetes in the year 2000 and it is expected to double by 2030.[4,5] India has already recognized as the diabetic capital of the world.[6]

Although the incidence of both type 1 and type 2 diabetes mellitus increasing but the pandemic principally involved by the type 2 diabetes.[4] It usually occurs after 30 years of age but peak ages is between 50 and 60 years. Recently this disease is seen in some younger than 20 years old probably due to increasing prevalence of obesity.[3]

The risk factors for the development of diabetes mellitus includes obesity (BMI >25 kg/m^2), Unsatisfactory diet, Physical inactivity, Race/ethnicity, Elderly people >40 years and Increasing urbanisation.[4,5]

In long standing cases it causes micro and macro vascular complications and degenerative changes in autonomic nervous system which leads to significant morbidity and mortality.[7,8]

Diabetic neuropathy is one of the microvascular complications of diabetes mellitus.

Nerve conduction studies are electrodiagnostics tests which are considered to be the most sensitive reliable noninvasive and objective means of investigating neuropathy.[9]

Hence the aim of present study was to study the motor and sensory nerve conduction parameters in type 2 diabetic patients and control group and compared with themselves.

Material and methods:

The present study was designed as case control study. This study was carried out in the department of Physiology at MGIMS, Sewagram, Wardha, Maharashtra after getting approved from institutional ethics committee. 100 subjects were included in this study, 50 type 2 diabetic patients as cases and 50 normal healthy subjects as controls. Patients were enrolled from department of Medicine after being diagnosed as diabetics. Diabetes Mellitus was diagnosed on the basis of Fasting Blood Sugar (FBS) >126 mg/dl [10] with appropriate signs and symptoms of type 2 diabetes mellitus.[11] Mean duration of diabetes was 5 years. Written Informed consent was obtained from all study participants. The exclusion criteria for this study were thyroid disorders, alcoholism, kidney diseases and those subjects who did not give consent.

The nerve conduction study was performed by RMS EMG EP MARK II, Chandigarh available in clinical neurophysiological unit, Department of Physiology in all subjects.

Motor nerve conduction studies were performed in median, ulnar, peroneal, and tibial nerves and Sensory nerve conduction studies were in median, ulnar and sural nerves. The studied parameters were distal motor latency (DML), amplitude (Amp) of compound muscle action potential (CMAP) and conduction velocity (CV) for motor nerve conduction study and amplitude (Amp) of sensory nerve action potential (SNAP) and conduction velocity (CV) for sensory nerve conduction study.

For recording CMAP of motor nerve conduction study surface disc electrodes were kept on abductor pollicis brevis for median nerve, abductor digiti minimi for ulnar nerve, extensor digitorum brevis for peroneal nerve and abductor hallucis longus for tibial nerves. Belly tendon montage was used with cathode and anode 3 cm apart. The stimulation was given at two different sites with maximum stimulus. Latency is the time between onset of stimulus to the initial CMAP deflection from baseline. CMAP amplitude is the difference between negative and positive peaks. The distance was measured and divided by conduction time between two points (difference between the proximal and distal motor latencies) which will give the conduction velocity. Ground electrode was placed between stimulating and recording electrodes.[12,13]

Sensory nerve conduction studies were recorded in median, ulnar and sural nerves. It was an antidromic sensory nerve conduction study. Surface electrodes were used and it was placed distally over the dermatomic distribution. Ground electrode was placed between stimulating and recording electrodes. Distance between active

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electrode and cathode of stimulator was divided automatically by onset latency to give sensory conduction velocity. SNAP amplitude was taken from peak to base.[12]

Statistical analysis was done by using z-test for difference between two means. The p value of less than 0.05 ($p<0.05$) was considered statistically significant. Data were expressed as mean±SD.

Results:-

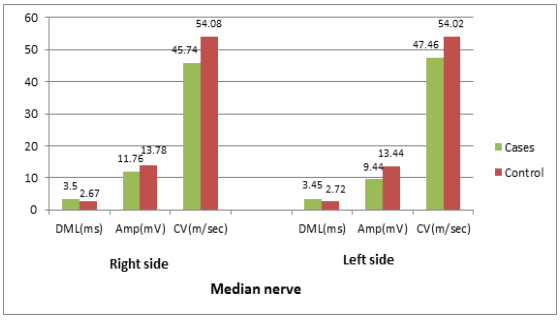
Alteration in motor and sensory nerve conduction parameters in type 2 Diabetes Mellitus and Controls are depicted below:-

Table 1: Showing comparison of Motor nerve conduction parameters of Upper Limb in patients of type 2 diabetes mellitus and controls

Median nerve				
	Parameters	Cases	Control	P Value
Right side	DML(ms)	3.50±0.66	2.67±0.32	0.0001 S,p<0.05
	Amp(mV)	11.76±5.77	13.78±3.50	0.037 S,p<0.05
	CV(m/sec)	45.74±7.57	54.08±4.09	0.0001 S,p<0.05
Left side	DML(ms)	3.45±0.83	2.72±0.22	0.0001 S,p<0.05
	Amp(mV)	9.44±3.72	13.44±2.92	0.0001 S,p<0.05
	CV(m/sec)	47.46±8.62	54.02±4.64	0.0001 S,p<0.05
Ulnar nerve				
	Parameters	Cases	Control	P Value
Right side	DML(ms)	2.40±0.86	2.17±0.31	0.075 NS,p>0.05
	Amp(mV)	11.17±2.30	11.00±1.99	0.69 NS,p>0.05
	CV(m/sec)	54.20±4.37	55.81±4.05	0.09 NS,p>0.05
Left side	DML(ms)	2.24±0.70	2.19±0.46	0.69NS,p>0.05
	Amp(mV)	10.47±2.79	10.97±3.12	0.39NS,p>0.05
	CV(m/sec)	54.84±9.75	55.88±4.48	0.49NS,p>0.05

S indicate as a level of significant statistically.
NS indicate as a level of non significant statistically.

Graph 1a: Showing comparison of Motor nerve conduction parameters in Median nerve in patients of type 2 diabetes mellitus and controls



Graph 1b: Showing comparison of Motor nerve conduction parameters in Ulnar nerve in patients of type 2 diabetes mellitus and controls

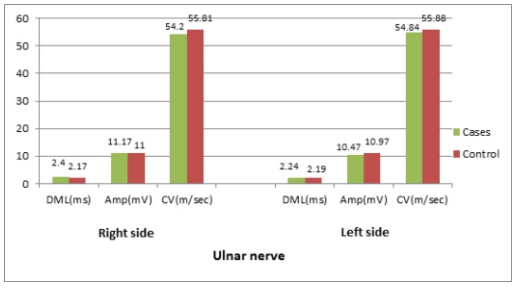
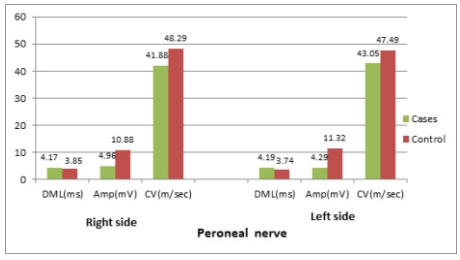


Table 2: Showing comparison of Motor nerve conduction parameters of Lower Limb in patients of type 2 diabetes mellitus and controls

Peroneal nerve				
	Parameters	Cases	Control	P Value
Right side	DML(ms)	4.17±1.04	3.85±0.48	0.047 S,p<0.05
	Amp(mV)	4.96±2.67	10.88±2.77	0.0001 S,p<0.05
	CV(m/sec)	41.88±7.69	48.29±6.13	0.0001 S,p<0.05
Left side	DML(ms)	4.19±0.70	3.74±0.46	0.0001 S,p<0.05
	Amp(mV)	4.29±2.63	11.32±3.03	0.0001 S,p<0.05
	CV(m/sec)	43.05±10.96	47.49±4.36	0.009 S,p<0.05
Tibial nerve				
	Parameters	Cases	Control	P Value
Right side	DML(ms)	3.96±0.54	3.63±0.63	0.007 S,p<0.05
	Amp(mV)	16.70±4.04	18.12±5.92	0.16 NS,p>0.05
	CV(m/sec)	42.49±10.38	49.11±7.63	0.0001 S,p<0.05
Left side	DML(ms)	4.32±0.87	3.81±0.60	0.001 S,p<0.05
	Amp(mV)	16.83±3.03	17.93±5.63	0.23 NS,p>0.05
	CV(m/sec)	40.25±14.01	49.97±7.56	0.0001 S,p<0.05

S indicate as a level of significant statistically.
NS indicate as a level of non significant statistically

Graph 2a: Showing comparison of Motor nerve conduction parameters in Peroneal nerve in patients of type 2 diabetes mellitus and controls



Graph 2b: Showing comparison of Motor nerve conduction parameters in Tibial nerve in patients of type 2 diabetes mellitus and controls

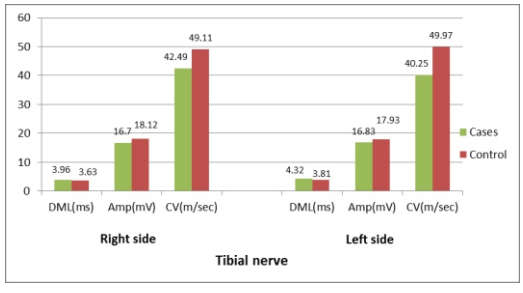


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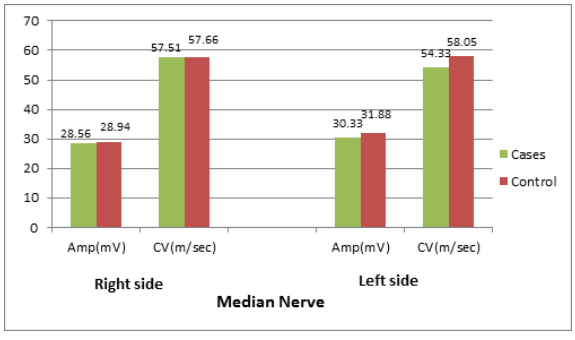
Table 3: Showing comparison of sensory nerve conduction parameters of Upper Limb in patients of type 2 diabetes mellitus and controls

Median nerve				
	Parameters	**Cases**	**Control**	**P Value**
Right side	Amp(μV)	28.56±17.30	28.94±19.82	0.91 NS,p>0.05
	CV(m/sec)	57.51±14.45	57.66±18.33	0.96 NS,p>0.05
Left side	Amp(μV)	30.33±16.30	31.88±24.93	0.71 NS,p>0.05
	CV(m/sec)	54.33±6.20	58.05±14.16	0.094 NS,p>0.05
Ulnar nerve				
	Parameters	**Cases**	**Control**	**P Value**
Right side	Amp(μV)	25.22±12.56	27.78±20.44	0.559 NS,p>0.05
	CV(m/sec)	57.94±24.94	59.39±14.20	0.489 NS,p>0.05
Left side	Amp(μV)	21.90±9.96	25.30±28.23	0.42 NS,p>0.05
	CV(m/sec)	52.33±11.81	55.98±9.51	0.094 NS,p>0.05

S indicate as a level of significant statistically.
NS indicate as a level of non significant statistically.

Graph 3a: Showing comparison of Sensory nerve conduction parameters in Median nerve in patients of type 2 diabetes mellitus and controls



Graph 3b: Showing comparison of Sensory nerve conduction parameters in Ulnar nerve in patients of type 2 diabetes mellitus and controls

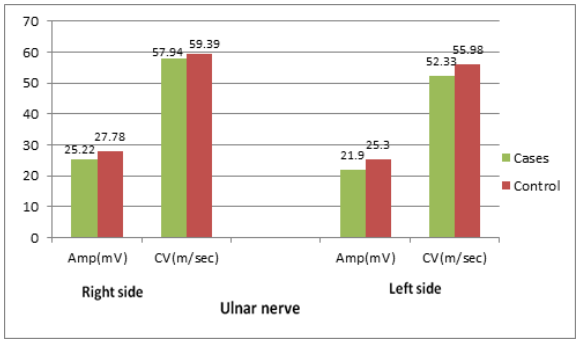
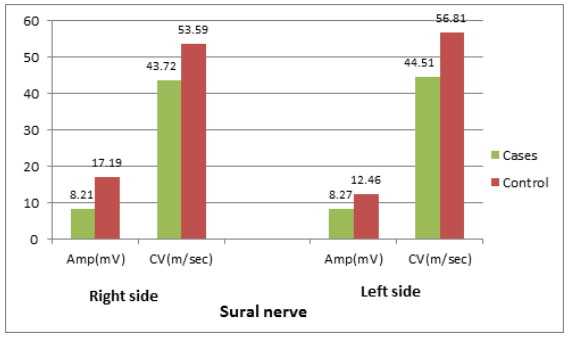


Table 4: Showing comparison of Sensory nerve conduction parameters of Lower Limb in patients of type 2 diabetes mellitus and controls

Sural nerve				
	Parameters	Cases	Control	P Value
Right side	Amp(μV)	8.21±1.12	17.19±7.28	0.0001 S,p<0.05
	CV(m/sec)	43.72±9.57	53.59±10.40	0.0001 S,p<0.05
Left side	Amp(μV)	8.27±1.78	12.46±4.31	0.0001 S,p<0.05
	CV(m/sec)	44.51±9.28	56.81±13.51	0.0001 S,p<0.05

S indicate as a level of significant statistically.
NS indicate as a level of non significant statistically.

Graph 4a: Showing comparison of Sensory nerve conduction parameters in Sural nerve in patients of type 2 diabetes mellitus and controls



Discussion:

In motor nerve conduction study we found that distal motor latencies were prolonged in cases compared to controls in bilateral median, peroneal and tibial nerves and differences were statistically significant.

Conduction velocities were decreased in cases compared to controls in bilateral median, peroneal and tibial nerves and differences were statistically significant. Further, Amplitudes were reduced in cases compared to controls in bilateral median and peroneal nerves and differences were statistically significant.

Amplitudes were also reduced in bilateral tibial nerve in cases compared to controls but differences were statistically not significant.

We also observed, distal motor latencies were prolonged and conduction velocities were decreased in bilateral ulnar nerve, amplitude was increased in right ulnar nerve and decreased in left ulnar nerve, however differences were statistically non significant .

In sensory nerve conduction study, amplitudes and conduction velocities were decreased in cases compared to controls in bilateral sural nerve and differences were statistically significant. Further amplitudes and conduction velocities were reduced in bilateral median and ulnar nerves in cases than controls but differences were statistically non significant.

Our findings supported by Gargate AR et al (2014)(14) who found significantly prolonged distal motor latency, reduced conduction velocity and amplitude in bilateral median and peroneal nerves and significant decrease in conduction velocity and amplitude in sural nerve of diabetic patients. But they also observed prolonged distal motor latency, reduced conduction velocity and amplitude in ulnar nerve which was not in accordance with our findings.

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Shinde K et al (2014)(15) also reported significant decreased in motor conduction velocity in median nerve in diabetic group with controlled as well as uncontrolled diabetes mellitus which was compatible with our findings.

Further, Mankar K et al (2016)(16) found significant reduction of conduction velocity and amplitude and prolonged distal motor latencies in bilateral median nerve in type 2 diabetic patients. In addition, they also observed significant reduction of conduction velocity in tibial nerve of type 2 diabetic patients and significant reduction of conduction velocity in sural nerve of diabetic patients.
Above findings indicate both motor and sensory neuropathy in diabetic patients. This neuropathy was of mixed variety i.e both axonal loss and demyelination.

Reduced amplitude is the primary abnormality associated with axonal loss. Amplitudes of CMAP and SNAP reflect the number of underlying motor and sensory nerve axons respectively. As axons are lost, the amplitudes of these potentials decrease.

Thus characteristic findings of axonal loss include:-
1. Reduce amplitude
2. Conduction velocities are normal or slightly decreased but never below 75% of the lower limit of normal and
3. Distal motor latencies are normal or slightly prolonged but never greater than 130% of the upper limit of normal.[13]
Myelin is essential for saltatory conduction. Disruption of normal saltatory conduction leads to marked slowing of conduction velocity or blocked.

On nerve conduction study, demyelination is associated with following features:-
1. Marked slowing of conduction velocity (slower than 75% of the lower limit of normal)
2. Marked prolongation of distal latency (longer than 130% of the upper limit of normal) or both.

Conduction velocities and latencies slower than these cutoff values imply primary demyelination, such values are not seen with axonal loss of the fastest conducting fibres. This is because there are simply no normal myelinated axons that conduct so slowly.[13]

So, decreased amplitude indicated axonal loss and slowing of conduction velocity and prolongation of distal latency indicated demyelination.

In our study we found prolonged distal motor latencies in motor nerve, reduced amplitude and conduction velocities in motor and sensory nerves. These findings suggest both axonal loss and demyelination in motor and sensory nerves. Further involvement of more than two nerves were observed in the present study which indicated polyneuropathy which literally means dysfunction of many or all peripheral nerves.[13]

Above findings suggests that diabetes mellitus, may present as motor or sensory polyneuropathy and it was of mixed variety i.e. both axonal loss and demyelination.

Peripheral neuropathy is one of the common complications of diabetes mellitus.[17]But the pathogenetic mechanisms responsible for diabetic neuropathy are poorly understood. Although there are several possible mechanisms by which nerve damage can occur, epidemiological and clinical data suggests that hyperglycemia and its metabolic consequences are responsible for the genesis of diabetic neuropathy.

Following are the possible mechanisms for the pathogenesis of diabetic
neuropathy:-
Hyperglycemia activates the enzyme aldose reductase by increasing its gene expression. Increase level of enzyme aldose reductase activates the polyol pathway which leads to intracellular accumulation of sorbitol and fructose. Accumulation of these osmolytes intracellularly is associated with reciprocal reduction of myoinositol, which in turn reduces cellular Na+-K+-ATPase activity as a result there is acute slowing of nerve conduction velocity and defects in axonal transport.[18,19]

Moreover activation of polyol pathway in the nerve through an enzyme aldose reductase induces non enzymatic glycosylation of structural nerve proteins which result in reduction of axonal transport. It reduces nerve function and shows an abnormal morphometry which leads to severe
morbidity.[17,19]

Elevated intracellular glucose as a result of hyperglycemia leads to cellular toxicity in the endothelial cells of the vasa nervosum. These intracellular glucose can also be converted to the so called Amadori product and these in turn form Advanced Glycosylated End product (AGE), a cross link matrix protein. These damages the blood vessels which results in ischaemia of the nerves and finally leads to neuropathy.[20] Further, elevated level of blood glucose increases endothelial vascular resistance and reduces blood flow to the nerves resulting in endothelial hypoxia. These hypoxia leads to further damage of the capillary which in turn aggravates disturbance in axonal transport and impairment of nerve conduction. Hyperglycemia also induces oxidative stress and activation of protein kinase C has been linked to vascular damage in diabetic neuropathy.[17]

Thus from our study we observed that Diabetes Mellitus is associated with development of generalised motor sensory polyneuropathy involving both axonal loss and demyelination. Hyperglycemia, vascular injury and other probable mechanisms play the important role in the pathogenesis of diabetic neuropathy.

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