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Original Article

Biochemistry Section

Association of HbA1c with Oxidative Stress and Peripheral Neuropathy in Newly Diagnosed Type 2 Diabetes Mellitus Cases: A Cross-sectional Study

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ABSTRACT

Introduction: Diabetic neuropathies are the most common, yet least understood and recognised long-term complications of diabetes. With rising Glycated Haemoglobins (HbA1c) levels, nerve conduction velocities slow and amplitudes decrease, indicating ongoing damage to the myelin sheaths and axonal loss. Worsening glycaemic control leads to increased Oxidative Stress (OS), which has been proposed to play a significant role in the progression of Diabetic Peripheral Neuropathy (DPN).

Aim: To evaluate peripheral nerve damage and Oxidative Stress levels in newly diagnosed Type 2 Diabetes Mellitus (T2DM) patients using Nerve Conduction Studies (NCS) and to assess their association with HbA1c levels.

Materials and Methods: The present cross-sectional analytical study was conducted on 60 newly diagnosed T2DM patients aged 40-60 years and 60 non-diabetic controls in the Department of Physiology, RG Kar Medical College and Hospital, Kolkata, West Bengal, India, from February 2023 to January 2024. Motor NCS were performed on the bilateral ulnar, median, and posterior tibial nerves, and sensory NCS were conducted on the bilateral median and sural nerves. OS levels were assessed by measuring the antioxidant enzyme catalase using spectrophotometry. Blood samples were collected for estimation of catalase activity, Fasting Blood Sugar (FBS), Postprandial Blood Sugar (PPBS), and HbA1c. Statistical analyses included Pearson's correlation coefficient and the unpaired t-test.

Results: Among the 60 patients (mean age 57 years; male:female ratio=1:1), 40% exhibited DPN. Distal motor latency of the bilateral median, ulnar, and tibial nerves was significantly increased in cases compared with controls. Motor nerve conduction velocity was significantly reduced in the patient group. Sensory nerve conduction velocity and sensory nerve action potential amplitudes of the bilateral sural nerves were decreased, while distal sensory latency was prolonged in cases compared with controls. A significant negative correlation was observed between HbA1c levels and catalase activity ($r= -0.78$, $p<0.0001$).

Conclusion: Newly diagnosed T2DM patients demonstrated significant abnormalities in nerve conduction parameters and a strong association between poor glycaemic control and OS. These findings suggest early nerve involvement and increased oxidative damage even at the time of diagnosis.

Keywords: Blood glucose, Catalase activity, Diabetic neuropathy, Glycated haemoglobins, Nerve conduction study, Sensory nerve latency

INTRODUCTION

Type 2 diabetes mellitus is a heterogeneous disorder characterised by varying degrees of insulin resistance, impaired insulin secretion, and increased hepatic glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the common phenotype of hyperglycaemia in T2DM [1]. In the 21st century, diabetes mellitus poses a major public health challenge due to the alarming increase in disease incidence, the high frequency of chronic microvascular complications (such as nephropathy and retinopathy), macrovascular complications (including stroke, coronary artery disease, and peripheral vascular disease), and the difficulties associated with optimal glycaemic control [2].

Diabetic peripheral neuropathy is defined as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" [3]. Diabetic neuropathy occurs in approximately 50% of individuals with long-standing T2DM and may present as polyneuropathy, mononeuropathy, or autonomic neuropathy [4]. Diabetic sensorimotor polyneuropathy is the most common form, with an estimated prevalence of nearly 50% [5]. As with other diabetic complications, the development of neuropathy correlates strongly with disease duration and glycaemic control and is associated with sensory loss, pain, and sometimes muscle weakness [6].

The initial mechanisms underlying neuropathy remain controversial, with several proposed hypotheses including excessive polyol pathway flux, nerve microangiopathy, non-enzymatic glycosylation of nerve proteins, early involvement of sensory and autonomic ganglia, deficiency of neurotrophic factors, OS, and nitric oxide toxicity [7]. Nerve conduction studies are considered among the most sensitive indicators of neuropathy severity and are useful for lesion localisation and characterisation of the underlying pathophysiological process [8]. Recent studies have demonstrated their utility in detecting neuropathic changes even during the preclinical stage [9,10]. Early diagnosis allows prompt intervention to prevent or delay complications.

Poor glycaemic control leads to increased OS, defined as an imbalance between Reactive Oxygen Species (ROS) production and antioxidant defence mechanisms [11]. Increased free radical production including nitric oxide, superoxide radicals, hydrogen peroxide, and hydroxyl radicals coupled with reduced antioxidant activity results in cellular damage through lipid peroxidation, protein oxidation, and DNA injury. The OS has been strongly implicated in the pathogenesis and progression of diabetic peripheral neuropathy, particularly in the setting of chronic hyperglycaemia. Antioxidants neutralise free radicals and reduce oxidative injury [12].

Catalase is a key antioxidant enzyme that catalyses the breakdown of Hydrogen Peroxide (H_2O_2) into water and oxygen. Reduced catalase activity leads to accumulation of ROS, thereby promoting oxidative stress and increasing susceptibility to neuropathy. Several antioxidants have been evaluated in experimental and clinical studies, including randomised trials of oral glutathione [13] and vitamin C and E supplementation in T2DM patients, which demonstrated improvements in glycaemic control and Oxidative Stress markers [14]. Against this background, the present study was conducted in Eastern India.

Study Objectives

1. To evaluate changes in NCS parameters of motor and sensory nerves in newly diagnosed T2DM patients compared with non-diabetic controls.
2. To assess changes in catalase activity as an OS marker in newly diagnosed T2DM patients compared with non-diabetic individuals.

MATERIALS AND METHODS

The present cross-sectional analytical study was conducted at RG Kar Medical Hospital, Kolkata, West Bengal, India, in the Department of Physiology, in collaboration with the Departments of Endocrinology, Biochemistry, and the Multidisciplinary Research Unit, from February 2023 to January 2024. Prior to commencement, ethical approval (registered with the Drug Controller General of India; Registration No. ECR/322/Inst/WB/2013/RR-20) was obtained from the Institutional Ethics Committee of RG Kar Medical College, Kolkata, West Bengal, India.

Inclusion criteria: Patients newly diagnosed with T2DM by the Endocrinology Outpatient Department (both males and females, aged 40-70 years) were included. Diagnosis was made according to American Diabetes Association (ADA) criteria in at least two consecutive blood samples [15], defined as: HbA1c >6.5%, or Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL), or Two-hour plasma glucose ≥11.1 mmol/L (200 mg/dL) following an oral glucose tolerance test, or In patients with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥11.1 mmol/L (200 mg/dL). Patients taking oral hypoglycaemic agents for less than one year were also eligible [16]. The control group included apparently healthy individuals of both sexes aged 40-70 years. Cases and controls were matched for age, height, and weight.

Exclusion criteria: Participants were excluded if they had any neuropathic disorder other than diabetic peripheral neuropathy, Cognitive impairment or inability to provide informed consent, unwillingness to undergo the tests, autoimmune disorders, alcohol dependence, Type 1 Diabetes Mellitus, use of neurotoxic drugs, malignancy, pregnancy or lactation, local ulcers on the limbs to be examined, implanted electronic devices (e.g., pacemakers), vitamin deficiencies (e.g., vitamin B12 deficiency), infections known to cause neuropathy (e.g., leprosy), drug-induced neuropathy (e.g., isoniazid), hereditary neuropathies (e.g., Charcot-Marie-Tooth disease), current use of antioxidant supplements.

Sample size calculation: DPN is the most common complication among patients with diabetes mellitus, with a reported prevalence ranging from 18.8% to 61.9% in India [17].

Sample size was calculated using the formula:

$n= (Z\alpha/2)^2\ pq/d^2$

So in the present study 'p' was taken to be 62%.

Margin of error (d) was taken to be 10%

Therefore, $n= \{(1.96)^2 \times 0.62 \times (1-0.62)\}/(0.1)^2= 90.5 \sim 90$ (rounded off to 120)

Where, $Z\alpha/2= 1.96$,

$p= 0.62$

$q= (1-p)= 0.38$

$d= 0.1$

Based on prevalence estimates, a total sample size of 120 was considered for this study. Sixty newly diagnosed T2DM patients aged 40-60 years and 60 non-diabetic controls were enrolled. Written informed consent was obtained, and detailed medical histories were recorded.

Study Procedure

Data collection: The study participants underwent the following assessments: a) NCS; b) Fasting Blood Sugar (FBS); c) PPBS; d) HbA1c; e) Catalase activity. All findings were documented in structured case record forms.

Nerve conduction: Motor nerve conduction studies were performed by electrical stimulation of peripheral nerves and recording from the muscles they innervate. Parameters measured included latency, amplitude, duration, area, and Conduction Velocity (CV).

Latency (ms) represents the time from stimulus onset to the initial deflection from baseline and reflects impulse transmission speed. Amplitude (mV), measured from baseline to peak, represents the number of functioning motor units. Conduction velocity (m/s) was calculated as:

CV= Distance (mm) / [Proximal latency (ms)-Distal latency (ms)]

Duration (ms) denotes the time from onset to peak, while area (mV·ms) represents the product of amplitude and duration, reflecting the density of conducting nerve fibres.

Sensory Nerve Action Potentials (SNAPs) were recorded by direct stimulation of sensory nerves, with measurement of latency, amplitude, duration, area, and conduction velocity.

Median motor nerve: The active electrode was placed over the belly of the abductor pollicis brevis muscle, and the reference electrode over the tendon approximately 3 cm distal at the first metacarpophalangeal joint. Stimulation was applied between the tendons of the flexor carpi radialis and palmaris longus (3 cm proximal to the distal wrist crease) for distal response, and at the elbow just medial to the brachial pulse for proximal response.

Median sensory nerve: Using the antidromic technique, recording ring electrodes were placed at the interphalangeal joints of the second digit. Stimulation was applied between the tendons of the flexor carpi radialis and palmaris longus, 3 cm proximal to the distal wrist crease [18].

Ulnar motor nerve: The active electrode was placed over the belly of the abductor digiti minimi muscle and the reference electrode 3 cm distal at the fifth metacarpophalangeal joint. Stimulation was applied at the medial wrist for distal response and behind the medial epicondyle at the elbow for proximal response [19].

Posterior tibial motor nerve: Participants lay in the prone position. The stimulating electrode was placed over the tibial nerve proximal to the flexor retinaculum. The active electrode was placed distally and the reference electrode proximally, with the ground electrode over the dorsum of the foot.

Sural sensory nerve: The sural nerve was stimulated antidromically 10-16 cm proximal to the recording electrode, distal to the lower border of the gastrocnemius muscle at the junction of the middle and lower thirds of the leg [18].

Catalase assay: Catalase activity was measured using a spectrophotometric method [19]. The decomposition of H_2O_2 was monitored at 240 nm. The reaction mixture contained 0.01 M phosphate buffer (pH 7.0), 0.02 M H_2O_2, and 20 µL of blood lysate. One unit of catalase activity was defined as the amount of enzyme decomposing 1 µmol of H_2O_2 per minute at 25°C.

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) software version 20. Unpaired Student's t-test and Pearson's correlation coefficient were applied. A p-value <0.05 was considered statistically significant.

RESULTS

Among the 60 newly diagnosed T2DM patients, 40% had developed peripheral neuropathy. In the present study, cases and controls were matched with respect to age, height, weight, and Body Mass Index (BMI). HbA1c levels were significantly higher in cases (8.05±1.90) compared with controls (5.52±0.35) (p <0.0001) [Table/Fig-1].

Parameters	Case (n=60)	Control (n=60)	p-value
Age (years)	58.59±12.72	55.95±7.85	0.16
Height (cm)	158.63±3.64	158.603.68	0.97
Weight (Kg)	56.33±2.44	56.35±2.43	0.98
BMI (Kg/m^2)	22.37±1.71	22.381.75	0.96
HbA1c (%)	8.05 ±1.90	5.52±0.35	<0.0001*

[Table/Fig-1]: Shows the baseline characteristics of the study subjects.
*A p-value <0.05 was taken to indicate significant difference

Distal Motor Latency (DML) of the bilateral median nerves was significantly increased in cases compared with controls (p <0.0001). DML of both the right tibial nerve (3.81±0.73) and left tibial nerve (3.95±0.53) was also significantly prolonged in cases (p <0.0001).

The amplitude of Compound Muscle Action Potential (CMAP) of the left median nerve was significantly reduced in cases (5.58±2.46) compared with controls (6.98±2.07). CMAP amplitudes of the bilateral ulnar nerves were also significantly decreased in cases (7.03±1.82 and 6.90±2.59) compared with controls (5.71±1.75 and 5.65±1.72, respectively) (p <0.0001).

Motor Nerve Conduction Velocity (MNCV) of the left median nerve was significantly reduced in cases (43.60±3.81) compared with controls (54.62±1.71). MNCV of the bilateral ulnar and tibial nerves was also significantly decreased in cases (p <0.0001) [Table/Fig-2].

Motor NCS parameters	Nerve	Cases (n=60)	Control (n=60)	p-value
DML (ms) of CMAP	Right median	4.15±0.56	2.79±0.57	<0.0001*
	Left median	3.91±0.52	2.62±0.24	<0.0001*
	Right ulnar	2.77±0.96	2.47±0.32	0.026
	Left ulnar	2.41±0.13	2.24±0.63	0.041
	Right tibial	3.81±0.73	3.36±0.30	<0.0001*
	Left tibial	3.95±0.53	3.25±0.07	<0.0001*
Amplitude (mV) of CMAP	Right median	5.59±2.82	5.49±2.22	0.82
	Left median	5.58± 2.46	6.98±2.07	<0.0001*
	Right ulnar	7.03± 1.82	5.71±1.75	<0.0001*
	Left ulnar	6.90±2.59	5.65±1.72	<0.0001*
	Right tibial	4.50±2.03	4.95±2.42	0.268
	Left tibial	4.67± 2.45	5.35±1.64	0.079
MNCV (m/s)	Right median	53.76±5.12	54.17±0.31	0.574
	Left median	43.60±3.81	54.62±1.71	<0.0001*
	Right ulnar	39.54±6.10	48.37±2.60	<0.0001*
	Left ulnar	40.75±4.51	47.65±2.91	<0.0001*
	Right tibial	41.81±2.71	52.08±1.47	<0.0001*
	Left tibial	41.04±2.59	49.68±2.33	<0.0001*

[Table/Fig-2]: Comparison of Distal Motor Latency (DML), Amplitude of Compound Muscle Action Potential (CMAP) and Motor Nerve Conduction Velocity (MNCV) of the motor nerves between cases and control subjects.
*A p-value <0.05 was taken to indicate significant difference

Distal Sensory Latency (DSL) of the SNAP of the right median nerve was significantly prolonged in cases (3.93±0.78) compared with controls (3.31±0.22). Distal sensory latency of the bilateral sural nerves was also significantly increased in cases (p <0.0001).

SNAP amplitude of the right median nerve was significantly decreased in cases (29.55±10.36) compared with controls (22.57±10.35), while SNAP amplitude of the right sural nerve was significantly reduced in cases (29.01±5.70) compared with controls (39.69±18.77) (p <0.0001). Sensory Nerve Conduction Velocity (SNCV) of the bilateral median and sural nerves was significantly reduced in cases compared with controls (p <0.0001) [Table/Fig-3].

Sensory nerve parameters	Nerve	Cases (n=60)	Control (n=60)	p-value
DSL (ms) of SNAP	Right median	3.31±0.22	3.93±0.78	<0.0001*
	Left median	3.21±0.56	3.37±0.86	0.236
	Right sural	4.07±0.29	2.55±0.35	<0.0001*
	Left sural	3.52±0.92	2.40±0.10	<0.0001*
Amplitude (mV) of SNAP	Right median	29.55±10.36	22.57±10.35	<0.0001*
	Left median	31.33±10.16	32.97±9.10	0.352
	Right sural	29.01±5.70	39.69±18.77	<0.0001*
	Left sural	21.45±5.01	20.60±4.55	0.332
SNCV (m/s)	Right median	49.45±2.79	57.99±3.6	<0.0001*
	Left median	44.1 ±7.11	57.63±2.67	<0.0001*
	Right sural	26.46±5.15	45.09±11.55	<0.0001*
	Left sural	26.62±4.03	42.23±12.88	<0.0001*

[Table/Fig-3]: Comparison of Distal Sensory Latency (DSL), Amplitude of Sensory Nerve Action Potential (SNAP) and Sensory Nerve Conduction Velocity (SNCV) of the sensory nerves between cases and control subjects.
*A p-value <0.05 was taken to indicate significant difference.

There was a significant positive correlation between HbA1c levels and Distal Motor Latency of the bilateral median, ulnar, and tibial nerves, and a significant negative correlation between HbA1c levels and CMAP amplitude and MNCV (p <0.0001) [Table/Fig-4].

Motor NCS parameters	Nerve	r-value	p-value
DML (ms) of CMAP	Right median	0.97	<0.0001*
	Left median	0.83	<0.0001*
	Right ulnar	0.82	<0.0001*
	Left ulnar	0.80	<0.0001*
	Right tibial	0.76	<0.0001*
	Left tibial	0.86	<0.0001*
Amplitude (mV) of CMAP	Right median	-0.86	<0.0001*
	Left median	-0.83	<0.0001*
	Right ulnar	-0.89	<0.0001*
	Left ulnar	-0.88	<0.0001*
	Right tibial	-0.83	<0.0001*
	Left tibial	-0.84	<0.0001*
MNCV (m/s)	Right median	-0.87	<0.0001*
	Left median	-0.82	<0.0001*
	Right ulnar	-0.86	<0.0001*
	Left ulnar	-0.79	<0.0001*
	Right tibial	-0.81	<0.0001*
	Left tibial	-0.83	<0.0001*

[Table/Fig-4]: Pearson correlation coefficient with HbA1c and Motor Nerve Conduction Study (NCS) parameters.
* A p-value <0.05 was taken to indicate significant difference

Similarly, distal sensory latency showed a significant positive correlation with HbA1c, while SNAP amplitude and SNCV

demonstrated significant negative correlations (p <0.0001) [Table/Fig-5].

Sensory nerve parameters	Nerve	r-value	p-value
DSL (ms) of SNAP	Right median	0.88	<0.0001*
	Left median	0.86	<0.0001*
	Right sural	0.89	<0.0001*
	Left sural	0.95	<0.0001*
Amplitude (mV) of SNAP	Right median	-0.93	<0.0001*
	Left median	-0.94	<0.0001*
	Right sural	-0.92	<0.0001*
	Left sural	-0.94	<0.0001*
SNCV (m/s)	Right median	-0.9	<0.0001*
	Left median	-0.93	<0.0001*
	Right sural	-0.94	<0.0001*
	Left sural	-0.94	<0.0001*

[Table/Fig-5]: Pearson correlation coefficient with HbA1c and sensory Nerve Conduction Study (NCS) parameters.
*A p-value <0.05 was taken to indicate significant difference

Blood catalase activity was significantly lower in T2DM patients (60.57±7.27 mU/L) compared with non-diabetic controls (97.78±11.36 mU/L) (p <0.0001) [Table/Fig-6]. Among diabetic patients, catalase activity was significantly lower in those with HbA1c ≥7% (58.36±5.70 mU/L) compared with those with HbA1c <7% (71.60±2.07 mU/L) (p <0.0001).

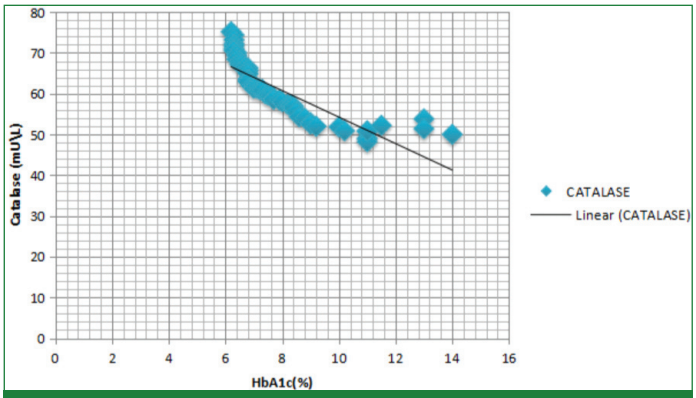
Parameter	Subject	Mean±SD	p-value
Catalase activity (mU/L)	Diabetics (n=60)	60.57±7.27	<0.0001*
	Non diabetics (n=60)	97.78±11.36	
Catalase activity (mU/L)	HbA1c <7% (n=10)	71.60±2.07	<0.0001*
	HbA1c ≥7% (n=50)	58.36±5.7	

[Table/Fig-6]: Showing comparison of catalase activity among cases and control.
*A p-value <0.05 was taken to indicate significant difference

Catalase activity showed a significant negative correlation with HbA1c (r=-0.78), fasting blood sugar (r=-0.885), and postprandial blood sugar (r=-0.990), all with p <0.0001. These relationships were also demonstrated in scatter plots [Table/Fig-7-10].

Catalase (mU/L)	HbA1c	FBS	PPBS
Pearson correlation	-0.784	-0.885	-0.990
p-value	<0.0001*	<0.0001*	<0.0001*

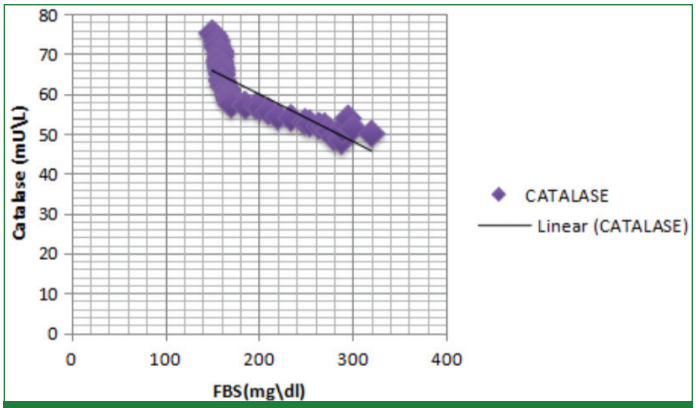
[Table/Fig-7]: Pearson correlation coefficient of Catalase with FBS, PPBS, HbA1c.
*A p-value <0.05 was taken to indicate significant difference



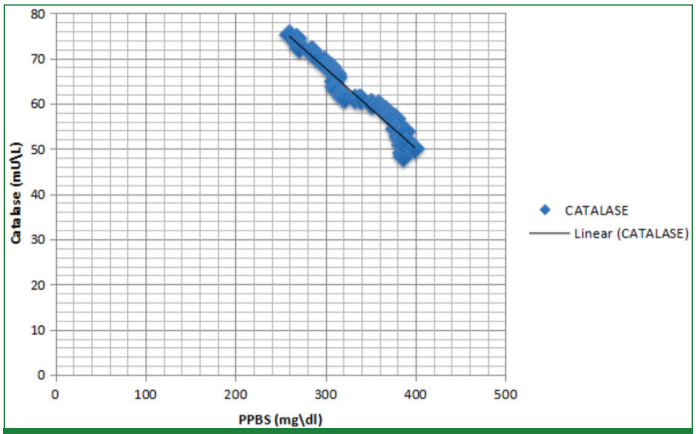
[Table/Fig-8]: Showing correlation of catalase with HbA1c.

DISCUSSION

DPN is a complex disorder resulting from impairment of multiple nerve fibre types in patients with diabetes. Electrophysiological studies, particularly nerve conduction studies, have emerged as valuable tools for detecting subclinical pathological changes in DPN.



[Table/Fig-9]: Showing correlation of Catalase with Fasting Blood Sugar (FBS).



[Table/Fig-10]: Showing correlation of catalase with Post Prandial Blood Sugar (PPBS).

In the present study, 120 participants of both sexes aged 40-60 years were recruited and matched for height, weight, and BMI. They were categorised into two groups: Group I comprised 60 newly diagnosed T2DM patients, and Group II included 60 healthy control subjects. Newly diagnosed patients were defined as those with T2DM receiving oral hypoglycaemic agents for less than one year [16].

The study demonstrated that 40% of newly diagnosed T2DM patients had developed peripheral neuropathy. Chopra JS and Hurwitz LJ similarly reported that more than 80% of asymptomatic recently diagnosed diabetic patients of one-year duration showed abnormal NCS findings [16].

Nerve conduction parameters of both motor and sensory nerves in the present study showed significantly increased latencies, reduced conduction velocities, and decreased amplitudes of CMAP and SNAP in newly diagnosed T2DM patients compared with healthy controls. These findings are consistent with previous reports [17].

Boulton AJM et al., also observed that even diabetic patients with good glycaemic control (HbA1c: 5.5-6.8%) exhibited increased latency and reduced amplitude and conduction velocity compared with non-diabetic individuals, with statistically significant differences [17].

In the present study, DML of the bilateral median and tibial nerves and DSL of the right median and bilateral sural nerves were significantly increased in cases compared with healthy control subjects. These findings are consistent with the study by Kimura J et al., which demonstrated increased latencies of the median, ulnar, and tibial nerves in diabetic patients compared with controls [20].

The present study also observed that the amplitude of CMAP of the left median nerve and bilateral ulnar nerves, as well as SNAP amplitude of the right median and right sural nerves, was significantly reduced in diabetic patients. These findings are supported by the study by Siddiqui AH et al., which reported significantly decreased SNAP and CMAP amplitudes in the median, posterior tibial, and sural nerves of diabetic subjects compared with controls [21].

Nerve conduction velocity of the left median, bilateral ulnar, tibial, and sural nerves was significantly lower in diabetic patients than in non-diabetic controls. This observation aligns with the study by Boulton AJM et al., who reported a progressive decline in nerve conduction velocity of approximately 1 m/s per year in diabetic neuropathy [17].

The present study demonstrated both demyelinating injury and axonopathy in diabetic neuropathy, as evidenced by increased latency, decreased amplitude, and slowed nerve conduction velocity. Increased latency typically reflects demyelination [22], and Chopra JS and Hurwitz LJ suggested that the early effects of diabetes on peripheral nerves are predominantly demyelinating [16]. Reduced amplitude is generally associated with axonal loss or dysfunction [23], as amplitude reflects the number of functioning axons within a nerve. Bansal V et al., also reported that slowing of nerve conduction velocity indicates progressive myelin damage and that decreasing amplitude with rising HbA1c suggests the onset of axonopathy [23].

A significant negative correlation was observed between HbA1c levels and nerve conduction parameters such as amplitude and conduction velocity ($p < 0.001$), along with a significant positive correlation between HbA1c and latency ($p < 0.001$). These findings corroborate the observations of Shaji RM et al., [24]. Lai YR et al., also reported reduced amplitudes in both motor and sensory nerve studies among patients with higher HbA1c levels [25]. Similarly, Peterson M et al., demonstrated a negative association between sural nerve amplitude and HbA1c levels [26]. The present study further found a significant negative correlation between HbA1c and sensory nerve conduction velocity, consistent with a 2019 Indian study [27].

The present study confirmed increased OS in newly diagnosed T2DM patients, as evidenced by significantly reduced catalase levels compared with non-diabetic controls. This finding is consistent with the report by Góth L [19], although previous studies have shown conflicting results regarding catalase activity in diabetes [28,29].

Furthermore, catalase activity was significantly lower in diabetic patients with poor glycaemic control (HbA1c ≥7%) compared with those with good glycaemic control (HbA1c <7%). This result contrasts with the findings of Sözmen B et al., who observed increased catalase activity in patients with higher HbA1c levels [30]. However, the significant negative association between HbA1c and catalase activity in the present study is consistent with the findings of Mandal M et al., who reported positive associations between hyperglycaemia and oxidative stress markers and negative associations with antioxidant levels [31].

Overall, the findings indicate that uncontrolled hyperglycaemia is associated with abnormal nerve conduction parameters and increased OS, both of which contribute significantly to the development of DPN. In hyperglycaemic conditions, OS promotes endothelial dysfunction and reduced capillary blood flow, leading to endoneurial hypoxia, neuronal apoptosis, and subsequent alterations in nerve conduction parameters [32,33].

Since diabetic neuropathy can be detected at a subclinical stage using nerve conduction studies and OS markers, these tests may be incorporated into routine diabetic evaluations for early intervention. Novel therapeutic strategies targeting OS, including antioxidant supplementation, may represent promising approaches for preventing or delaying neuropathy progression. However, further large-scale studies in the Eastern Indian population are required to validate these findings.

Limitation(s)

As the present study was a cross-sectional study, causal relationships between variables could not be established; only associations were identified. The sample size was limited to a single institution, which may affect the generalisability of the results. Additionally, the relatively short study duration may have influenced data collection and analytical depth.

CONCLUSION(S)

The DPN was present in 40% of newly diagnosed T2DM patients. HbA1c levels showed significant associations with several nerve conduction parameters, indicating early neural impairment even at diagnosis. Catalase activity demonstrated significant negative correlations with FBS, PPBS, and HbA1c, supporting the role of OS in neuropathy development. Future multicentric studies with larger sample sizes are required to further elucidate these relationships and explore the potential therapeutic benefits of antioxidant strategies in diabetic neuropathy.

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