Study the role of dyslipidemia in cases of neuropathy with type 2 diabetes mellitus

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Background
Diabetic neuropathy is one of the most common neurological diseases. Dyslipidemia is very common in diabetic patients and thought to add to the effect of diabetes on peripheral nerves.
Objectives
To assess the effect of dyslipidemia on diabetic peripheral neuropathy among patients with type 2 diabetes mellitus.
Patients and methods
A total of 60 patients with peripheral diabetic polyneuropathy were included and divided into two groups: the first included 30 patients with diabetic neuropathy and dyslipidemia and the other 30 patients had diabetic neuropathy without dyslipidemia. Another 30 healthy volunteers were included as a control group. All were subjected to full history taking, clinical examination, laboratory investigations, and neurophysiological studies.
Results
Hypertension and smoking were significantly increased in cases when compared with controls. Regarding the severity of neuropathy, it was mild in seven (11.7%) patients, moderate in 34 (56.7%) patients, and severe in 19 (31.7%) patients. Neurophysiological studies of the studied populations revealed significant changes of both motor and sensory parameters in cases when compared with controls and in the group with dyslipidemia when compared with the group without dyslipidemia. In addition, there was a significant correlation between lipid profile and each of glycated hemoglobin, fasting and postprandial blood sugar, and different neurophysiological examinations.
Conclusion
Dyslipidemia added to the hazardous effect of diabetic neuropathy on neurophysiological studies. In addition, there was a significant correlation between lipid profile and changes in nerve conduction studies.

Keywords:
amplitude, conduction velocity, dyslipidemia, nerve conduction studies, neuropathy

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Introduction

Diabetic peripheral neuropathy (DPN) is a frequent complication of type 2 diabetes mellitus (DM), with an estimated prevalence of 8% in newly detected cases of diabetes and more than 50% in cases with a long evolution of the disease [1]. Currently, there is no cure, and management primarily comprises symptom relief. So, there is a need for early identification and detection of etiological factors that underlie DPN development and that can provide avenues for preventive care [2].

Despite tight glycemic control, diabetic neuropathy continues to develop as a microvascular complication in a significant proportion of diabetic patients, especially type 2 DM [3]. The progress of diabetic neuropathy is accompanying by several modifiable and nonmodifiable risk factors like hypertension, dyslipidemia, insulin resistance, obesity, cigarette smoking, and alcohol drinking in addition to the degree of hyperglycemia [4].

The exact role of cholesterol metabolism in the development of DPN is controversial. Some clinical studies have found that a lowering of serum cholesterol levels had a positive effect on the course of DPN, which is mainly attributed to the lowering of low-density lipoprotein (LDL) cholesterol levels and to anti-inflammatory and antioxidative effects of statin treatment [5]. However, other clinical studies have found that low serum cholesterol levels are related to neuropathic symptoms and impairment nerve regeneration after axonal damage in neurons of the

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central and peripheral nervous systems [6,7]. This association was mainly attributed to an insufficient supply of cholesterol to neurite tips and adjacent Schwann cells of regenerating axons as a consequence of a decrease in lipoproteins [8]. The aim of the study was to assess the effect of dyslipidemia on DPN among patients with type 2 DM.

Patients and methods

A case–control study was conducted at the Neurophysiology Unit of Neurology Department and Internal Medicine Department at Al-Azhar University Hospital, New Damietta, Egypt. The study was approved by the local ethical committee of Damietta faculty of medicine Al-Azhar University, on the 13th of January 2019. Before participation in the study, the study procedure was clarified for each subject, and informed consent from participants was provided by each person. The study was conducted on two groups of patients presented clinically with diabetic peripheral polyneuropathy and diagnosed according to diagnostic criteria [9] (bilateral, symmetrical, distal motor, and sensory impairment, with a graded increase in severity distally; it was manifested with pain, tingling, numbness, and muscle weakness) who were referred from the outpatient clinic of neurology of Al-Azhar University Hospital, New Damietta, Egypt. Each group included 30 patients, where one of the groups included patients with hyperlipidemia. Moreover, the study included 30 healthy participants as a control group.

Inclusion criteria

All patients having diabetic polyneuropathy were included. The patients with type 2 DM were previously diagnosed according to the following: history of type DM, patients receiving antidiabetic medications, fasting blood glucose more than or equal to 126 mg/dl, 2 h postprandial blood glucose more than or equal to 200 mg/dl, and glycated hemoglobin (HbA1c) more been 6.5% [10]. Dyslipidemia was diagnosed according to LDL more than or equal to 140 mg/d;, triglycerides (TGs) more than or equal to 150 mg/dl, cholesterol more than 240 mg/dl, and high-density lipoprotein (HDL) less than 140 mg/dl [11].

Exclusion criteria

Exclusion criteria were as follows: (a) all patients having radiculopathy; (b) severe systemic diseases rather than DM or hyperlipidemia, like alcoholism, liver cell failure, and chronic kidney disease; and (c) type 1 DM.

All included patients were subjected to the following: full history taking, neurological examination, laboratory investigations, and neurophysiological examination. The clinical diagnosis of polyneuropathy was done according to the diagnostic criteria of Hanewinckel *et al.* [9] (symmetrical, bilateral distal motor and sensory impairment with a graded increase in severity distally; it was manifested with pain, tingling, numbness, and muscle weakness). The assessment of the severity of polyneuropathy in the patients was done by total neuropathy symptom score [12]. Neuropathy symptom score consist of five questions. Each question was assessed with points (p) in order to calculate the total symptom score. The total symptom score was calculated and converted into grade of symptom: 3–4 points were converted into mild symptoms, 5–6 points into moderate symptoms, and 7–9 points into severe symptoms.

(1) Burning, numbness, and tingling (2p) or fatigue, cramping, and aching (1p) feelings in the lower extremity.
(2) The feelings (symptoms) are present in the feet (2p) or calf (1p).
(3) There are nocturnal exacerbations of the feelings (symptoms) (2p) or they are equally present during the day and night (1p).
(4) The feelings (symptoms) wake the patient up from sleep (1p).
(5) Walking (2p) or standing (1p) maneuvers reduce symptoms.

In addition, the neurophysiological examination for all patients and control was done according to the protocol of polyneuropathy as described by Wisotzky *et al.* [13].

Electrophysiological studies were performed using Nihon Kohden Machine, model UT-0800J, Box BOARD (2CH) for JB-942BK (Japan), at the Neurophysiology Department of Al-Azhar University Hospital, New Damietta, Egypt.

General principles

Sensory and motor nerve conduction studies (NCSs) were performed with surface stimulation and recording of the compound muscle action potential from the surface electrode. Cleaning of the site for examination was done with alcohol. Ground is placed between the stimulating and recording electrodes.

Nerve conduction studies (NCSs)

(A) Motor nerve conduction: Motor NCS are performed by electrical stimulation of a peripheral

nerves (tibial, peroneal and median) and recording motor latency, amplitude and conduction velocity from a muscle supplied by these nerves (abductor hallucis brevis, extensor digitorum brevis and abductor pollicis brevis) and the ground electrode: Placed between recording electrode and the stimulator.

(B) Sensory nerve conduction (antidromic): Sensory NCS are performed by electrical stimulation of a peripheral nerves (sural and median) and recording sensory latency, and amplitude from a purely sensory portion of the nerve, (area behind and below lateral malleolus and index finger) and the ground electrode: Placed on the dorsum of the hand between recording electrode and the stimulator. Motor NCSs were performed by electrical stimulation of peripheral nerves (tibial, peroneal, and median) and recording of motor latency, amplitude, and conduction velocity (CV) from a muscle supplied by these nerves (abductor hallucis brevis, extensor digitorum brevis, and abductor pollicis brevis) and the ground electrode, which was placed between recording electrode and the stimulator.

Electrophysiological studies interpretation data

(1) Criteria for demyelinating polyneuropathy are based on the need of three of the following four factors: prolonged distal latency in two or more nerves not at entrapment sites (distal latency >130% upper lower normal), CV slowing in two or more nerves not at entrapment sites (CV <75% lower limit normal), prolonged late response (>130% upper lower normal), and conduction block or temporal dispersion in one or more nerves [definite conduction block if distal compound motor action potential (CMAP) is less than 50% area of proximal CMAP] [13].
(2) Criteria for axonal polyneuropathy: if borderline CV with low amplitudes in two or more nerves.

The following laboratory investigations were done: lipid profile (TGs, cholesterol, HDL, LDL), random blood sugar, postprandial plasma glucose, liver and renal function tests, and HbA1c.

Statistical analysis

The collected data were organized, tabulated, and statistically analyzed using statistical package for the social sciences (SPSS), version 16 (SPSS Inc., Chicago, Illinois, USA). Numerical data were presented as mean ±SD, whereas categorical data were presented as frequency and percent. Comparison among groups was done by independent samples (t) test for two means and multivariate analysis of variance (MANOVA) for comparing multivariate sample means with least significant differences as post-hoc analysis. Comparison among groups of categorical variables was done by χ^2 test or Mann–Whitney test when appropriate. In addition, correlation between two variables was done by estimation of Pearson correlation coefficient (r); it is considered mild if r less than 0.3, moderate if r more than 0.3, and less than 0.7 and powerful if r more than 0.7. It was proportional if the sign is positive and inverse if the sign is negative. P value less than 0.05 was considered significant for interpretation of results.

Results

The study was conducted on two groups of diabetic patients with polyneuropathy: group 1 comprised diabetes with hyperlipidemia, and group 2 comprised diabetes without hyperlipidemia. Moreover, 30 healthy participants were included as a control group. All patients were referred from the outpatient clinics of neurology and internal medicine of Al-Azhar University Hospital, New Damietta, Egypt. Patient groups and control were comparable regarding age and sex. The mean age was 50.93±4.49 years. Males represented 13 in group 1, 15 in group 2, and 16 in the control group. There was a statistically significant increase of hypertension and smoking in group 1 when compared with group 2 or group 3 (Table 1).

Regarding the severity of neuropathy according to total neuropathy symptom scale, it was mild in seven (11.7%) patients, moderate in 34 (56.7%) patients, and severe in 19 (31.7%) patients, and there was a significant increase of severe neuropathy in group 1 when compared with group 2.

Table 1 General characteristics of the studied populations

Variables	Group 1 [n (%)]	Group 2 [n (%)]	Group 3 [n (%)]	Test	P value
Age	50.93±4.49	50.93±3.68	51.50±3.85	0.19	0.82
Sex					
Male	13 (43.3)	15 (50.0)	16 (53.3)	0.62	0.73
Female	17 (56.7)	15 (50.0)	14 (46.7)		
Hypertension	16 (53.3)	1 (3.3)	0	34.95	<0.001*
Smoking	11 (36.7)	1 (3.3)	0	21.34	<0.001*

*Significant.

Cholesterol and TGs were significantly increased in group 1 when compared with groups 2 and 3. There was a statistically significant increase of LDL and HDL in group 1 when compared with other two groups.

The motor conduction study of median, tibial, and peroneal nerves as a result of MANOVA for comparing multivariate sample means with least significant differences as post-hoc analysis showed the following: statistically significant prolongation of terminal latency in groups 1 and 2 when compared with control group, and the prolongation of terminal latency in group 1 is more when compared with group 2; a statistically significant reduction of amplitude of CMAP of the examined motor nerves, except the right peroneal nerve, in groups 1 and 2 when compared with control group, but without statistically difference of reduction of amplitude of CMAP in group 1 when compared with group 2; and a statistically significant reduction of CV in groups 1 and 2 when compared with control group, and the reduction of CV in group 1 is more when compared with group 2 (Tables 2 and 3).

The sensory conduction study of median and sural nerves and as a result MANOVA for comparing multivariate sample means with least significant differences as post-hoc analysis showed the following: there was a statistically significant prolongation of terminal latency in groups 1 and 2 when compared with control group, and the prolongation of terminal latency in group 1 is more when compared with group 2, and also there was a statistically significant reduction of amplitude of sensory nerve action potential of examined nerves in groups 1 and 2 when compared with control group but without statistically difference of reduction of amplitude of CMAP in group 1 when compared with group 2 (Tables 4 and 5).

Axonal polyneuropathy was present in 12 patients, representing two patients in group 1 and 10 patients in group 2. Demyelinating polyneuropathy was present in 15 patients, representing eight patients in group 1 and seven in group 2, and mixed polyneuropathy was present in 33 patients, representing 20 in group 1 and 13 in group 2. There was a statistically significant increase in mixed neuropathy in group 1 when compared with group 2. The control group had no neuropathy.

There was a significant negative (inverse) correlation between HDL and each of HbA1c, fasting blood glucose, and postprandial blood glucose, whereas

Table 2 Comparison among studied groups regarding motor nerve neurophysiological studies

	Group 1		Group 2		Control		*F*	*P*
	Mean	SD	Mean	SD	Mean	SD		
Right median nerve								
Latency (ms)	8.87	0.82	5.08	1.27	3.81	0.27	41.367	0.000*
Amplitude (mV)	3.76	0.86	3.57	0.97	5.87	1	55.05	0.000*
CV (m/s)	30.4	6.87	38.07	13.28	57.24	4.73	69.978	0.000*
Left median nerve								
Latency (ms)	5.87	0.82	5.08	1.27	3.81	0.27	41.37	0.000*
Amplitude (mV)	3.76	0.86	3.57	0.97	5.92	1.02	56.89	0.000*
CV (m/s)	30.4	6.86	38.06	13.28	57.24	4.74	69.98	0.000*
Right tibial nerve								
Latency (ms)	7.17	0.47	6.52	1.09	5.73	0.32	31.013	0.000*
Amplitude (mV)	3.8	1.04	3.62	1.09	5.74	0.58	48.81	0.000*
CV (m/s)	30.65	5.68	36.47	9.88	52.39	4.67	75.193	0.000*
Left tibial nerve								
Latency (ms)	7.17	0.47	6.52	1.09	5.73	0.33	30.68	0.000*
Amplitude (mV)	3.76	1.03	3.62	1.09	5.76	0.57	49.79	0.000*
CV	30.65	5.68	36.43	9.83	52.4	4.67	75.72	0.000*
Right peroneal nerve								
Latency (ms)	7.44	0.98	6.34	0.81	4.58	0.85	38.073	0.000*
Amplitude (mV)	1.12	0,83	0.97	0.67	2.88	0.62	61.335	0.000*
CV (m/s)	24.85	8.4	32.37	13.29	48.19	9.02	38.915	0.000*
Left peroneal nerve								
Latency (ms)	7.44	0.97	6.34	1.8	4.61	0.87	36.86	0.000*
Amplitude (mV)	1.12	0.83	0.97	0.77	11.39	46.77	1.466	<0.236
CV (m/s)	24.85	8.38	32.37	13.29	49.61	3.86	55.38	0.000*

CV, conduction velocity. *Significant.

Table 3 Post-hoc test for comparison among studied groups regarding motor nerve neurophysiological studies

	Control (I)–group 1 (J)					Control (I)–group 2 (J)					Group 1 (I)–group 2 (J)				
				95% confidence interval					95% confidence interval					95% confidence interval	
Variables	Mean difference	SE	Significance	Lower bound	Upper bound	Mean difference (I–J)	SE	Significance	Lower bound	Upper bound	Mean difference (I–J)	SE	Significance	Lower bound	Upper bound
Amplitude of peroneal (mV)															
Right	1.7620*	0.19217	0.000	1.3038	2.2202	1.9150*	0.19217	0.000	1.4568	2.3732	0.1530	0.19217	0.706	–0.3052-	0.6112
Terminal latency of peroneal (ms)															
Right	–2.8573*	0.33049	0.000	–3.6454	–2.0693	–1.7670*	0.33049	0.000	–2.5550	–0.9790	1.0903*	0.33049	0.004	0.3023	1.8784
Left	–2.8250*	0.33184	0.000	–3.6163	–2.0337	–1.7347*	0.33184	0.000	–2.5259	–0.9434	1.0903*	0.33184	0.004	0.2991	1.8816
Conduction velocity of peroneal (m/s)															
Right	23.3397*	2.70067	0.000	16.9000	29.7794	15.8163*	2.70067	0.000	9.3766	22.2560	–7.5233*	2.70067	0.018	–13.9630	–1.0836
Left	24.7567*	2.41193	0.000	19.0055	30.5079	17.2333*	2.41193	0.000	11.4821	22.9845	–7.5233*	2.41193	0.007	–13.2745	–1.7721
Amplitude of tibial (mV)															
Right	1.9847*	0.24003	0.000	1.4123	2.5570	2.1167*	0.24003	0.000	1.5443	2.6890	0.1320	0.24003	0.847	–0.4403	0.7043
Left	1.9997*	0.23938	0.000	1.4289	2.5705	2.1317*	.23938	0.000	1.5609	2.7025	0.1320	0.23938	0.846	–0.4388	0.7028
Terminal latency of tibial (ms)															
Right	–1.4422*	0.18346	0.000	–1.8797	–1.0048	–0.7967*	0.18346	0.000	–1.2341	–0.3592	0.6456*	0.18346	0.002	0.2081	1.0830
Left	–1.4370*	0.18374	0.000	–1.8751	–0.9989	–0.7914*	0.18374	0.000	–1.2296	–0.3533	0.6456*	0.18374	0.002	0.2074	1.0837
Conduction velocity of tibial (m/s)															
Right	21.7370*	1.83533	0.000	17.3607	26.1133	15.9233*	1.83533	0.000	11.5470	20.2996	–5.8137*	1.83533	0.006	–10.1900	–1.4374
Left	21.7503*	1.83096	0.000	17.3844	26.1162	15.9700*	1.83096	0.000	11.6041	20.3359	–5.7803*	1.83096	0.006	–10.1462	–1.4144
Amplitude of median (mv)															
Right	2.1153*	.24369	0.000	1.5343	2.6964	2.3017*	0.24369	0.000	1.7206	2.8827	0.1863	0.24369	0.726	–0.3947	0.7674
Left	2.1687*	0.24546	0.000	1.5834	2.7539	2.3550*	0.24546	0.000	1.7697	2.9403	0.1863	0.24546	0.729	–0.3989	0.7716
Terminal latency of median (ms)															
Right	–2.0627*	0.22884	0.000	–2.6083	–1.5170	–1.2750*	0.22884	0.000	–1.8207	–0.7293	0.7877*	0.22884	0.003	0.2420	1.3333
Left	–2.0627*	0.22884	0.000	–2.6083	–1.5170	–1.2750*	0.22884	0.000	–1.8207	–0.7293	0.7877*	0.22884	0.003	0.2420	1.3333
Conduction velocity of median (m/s)															
Right	26.8360*	2.33707	0.000	21.2633	32.4087	19.1793*	2.33707	0.000	13.6066	24.7520	–7.6567*	2.33707	0.004	–13.2294	–2.0840
Left	26.8360*	2.33707	0.000	21.2633	32.4087	19.1793*	2.33707	0.000	13.6066	24.7520	–7.6567*	2.33707	0.004	–13.2294	–2.0840

Based on observed means. The error term is mean square (error)=0.489. *The mean difference is significant at the 0.05 level.

Table 4 Comparison among studied groups regarding sensory nerve neurophysiological studies

	Group 1		Group 2		Control		*F*	*P*
	Mean	SD	Mean	SD	Mean	SD		
Right median sensory								
Latency (ms)	4.69	0.61	4.04	1.2	2.87	0.22	52.263	0.000*
Amplitude (μv)	13.31	7.73	11.73	7.24	21.97	3.26	22.308	0.000*
Left median sensory								
Latency (ms)	4.69	0.62	4.05	1.02	2.87	0.21	52.661	0.000*
Amplitude (μv)	13.25	7.62	11.70	7.25	21.99	3.17	22.948	0.000*
Right sural nerve								
Latency (ms)	5.65	0.42	5.05	0.99	3.5	0.63	70.186	0.000*
Amplitude (μv)	3.7	1.53	3.54	2.1	8.4	2.25	57.415	0.000*
Left sural nerve								
Latency (ms)	5.66	0.43	5.04	1	3.47	0.61	73.193	0.000*
Amplitude (μv)	4.39	3.70	3.55	2.1	8.4	2.44	21.287	0.000*

*Significant.

there was a positive correlation between LDL and each of HbA1c, fasting blood glucose, and postprandial blood glucose (Table 6).

There were positive correlations between each of cholesterol, TG, and LDL with motor latency and correlated negatively with each of motor amplitude and CV in all studied nerves. Instead, HDL was negatively correlated with latency and positively correlated with each of amplitude and CV of all studied nerves (Table 7).

Each of the cholesterol, TG, and LDL were positively correlated with sensory latency and correlated negatively with sensory amplitude in all studied nerves. On the contrary, HDL was negatively correlated with latency and positively correlated with amplitude of all studied nerves (Table 8).

There was a statistically significant positive correlation between disease severity and mixed axonal demyelinating polyneuropathy (Table 9). Regarding the severity of neuropathy, there was a statistically significant positive correlation between disease severity and the dyslipidemia (Table 10).

Discussion

In the present study, hypertension was reported in 17 (28.3%) patients and smoking was reported in 12 (20.0%) patients. There was a significant increase of hypertension and smoking in patients when compared with the control group. However, the difference regarding age and sex was statistically nonsignificant. These results are comparable to those reported by Tesfaye *et al.* [14]; they reported that vascular risk factors have been identified as potential neuropathy risk factors in diabetic and nondiabetic populations. The EURODIAB study followed 1172 patients with diabetes and found that incident neuropathy risk was increased by both glycemic control and other vascular risk factors including hypertriglyceridemia, hypertension, obesity, and tobacco use. In addition, Anari *et al.* [15] reported that approximately half of the participants had hypertension.

In the present study, the motor conduction study of median, tibial, and peroneal nerves in the patient group showed prolonged terminal latency and reduced amplitude of CMAP and CV when compared with control group. In addition, the sensory conduction study of the median and sural nerves in the patient group showed prolonged terminal latency and reduced amplitude of sensory nerve action potential when compared with the control group. These results are comparable to those reported by De Souza *et al.* [16]; they reported that their study demonstrates that DPN is characterized by prolonged distal and proximal CMAP latencies in the median and peroneal nerves, with slowed motor nerve conduction velocity (NCV). Distal and proximal motor amplitudes were lowered in the lower limb but not in upper limb nerves when compared with normal, and even presymptomatic diabetics had a highly significant slowing of motor NCV. Motor latencies were prolonged with further slowing of NCV in the symptomatic group, and a reduction of CMAP amplitudes compared with the asymptomatic group.

In the present work, there was a statistically significant increase of cholesterol, TGs, and LDL and a significant decrease of HDL in cases when compared with controls, and there was a statistically significant increase of cholesterol, TGs, and LDL in study group 1 when compared with group 3. On the contrary, there was a statistically significant decrease in HDL in group 1 when

Table 5 Post-hoc test for comparison among studied groups regarding sensory nerve neurophysiological studies

Variable	Control (I)–group 1 (J)					Control (I)–group 2 (J)					Group 1 (I)–group 2 (J)				
	Mean difference	SE	Significance	95% confidence Interval		Mean difference (I–J)	SE	Significance	95% confidence Interval		Mean difference (I–J)	SE	Significance	95% confidence Interval	
				Lower bound	Upper bound				Lower bound	Upper bound				Lower bound	Upper bound
Amplitude of sural (μv)															
Right	4.6630*	0.51333	0.000	3.4390	5.8870	4.8587*	0.51333	0.000	3.6346	6.0827	0.1957	0.51333	0.923	−1.0284	1.4197
Left	3.6497*	0.73177	0.000	1.9048	5.3946	4.4910*	0.73177	0.000	2.7461	6.2359	0.8413	0.73177	0.486	−0.9036	2.5862
Terminal latency of sural (ms)															
Right	−2.1440*	0.18666	0.000	−2.5891	−1.6989	−1.5417*	0.18666	0.000	−1.9868	−1.0966	0.6023*	0.18666	0.005	0.1572	1.0474
Left	−2.1840*	0.18607	0.000	−2.6277	−1.7403	−1.5650*	0.18607	0.000	−2.0087	−1.1213	0.6190*	0.18607	0.004	0.1753	1.0627
Amplitude of median (μv)															
Right	8.6627*	1.65172	0.000	4.7242	12.6012	10.2483*	1.65172	0.000	6.3098	14.1868	1.5857	1.65172	0.604	−2.3528	5.5242
Left	8.7407*	1.63785	0.000	4.8352	12.6461	10.2897*	1.63785	0.000	6.3842	14.1951	1.5490	1.63785	0.613	−2.3564	5.4544
Terminal latency of median (ms)															
Right	−1.8193*	0.18056	0.000	−2.2499	−1.3888	−1.1807*	0.18056	0.000	−1.6112	−0.7501	0.6387*	0.18056	0.002	0.2081	1.0692
Left	−1.8277*	0.18064	0.000	−2.2584	−1.3969	−1.1827*	0.18064	0.000	−1.6134	−0.7519	0.6450*	0.18064	0.002	0.2143	1.0757

Based on observed means. The error term is mean square (error)=0.489. *The mean difference is significant at the 0.05 level.

Table 6 Correlation between lipid profile and laboratory investigations

	Cholesterol	Triglycerides	HDL	LDL
Glycated hemoglobin	−0.113	−0.007	−0.372**	0.288**
Fasting blood glucose	−0.105	−0.033	−0.355**	0.298**
Postprandial blood glucose	−0.050	0.044	−0.406**	0.299**

HDL, high-density lipoprotein; LDL, low-density lipoprotein.
**Highly significant.

Table 7 Correlation between lipid profile and motor nerve conduction

	Cholesterol	Triglycerides	HDL	LDL
Right median nerve				
Latency	0.318**	0.411**	−0.536**	0.402**
Amplitude	−0.018	−0.176	0.174	−0.076
CV	−0.214*	−0.354**	0.471**	−0.358**
Left median nerve				
Latency	0.209*	0.245**	−0.212*	0.080
Amplitude	−0.056	−0.196*	0.197*	−0.102
CV	−0.225*	−0.360**	0.486**	−0.357**
Right tibial nerve				
Latency	0.208*	0.324**	−0.474**	0.319**
Amplitude	−0.178	−0.306**	0.335**	−0.187*
CV	−0.360**	−0.356**	0.427**	−0.358**
Left tibial nerve				
Latency	0.424**	0.556**	−0.545**	0.339**
Amplitude	−0.234*	−0.306**	0.252**	−0.155
CV	−0.301**	−0.313**	0.421**	−0.274**
Right peroneal nerve				
Latency	0.053	0.137	−0.324**	0.231*
Amplitude	−0.158	−0.229*	0.321**	−0.135
CV	−0.050	−0.144	0.378**	−0.278**
Left peroneal nerve				
Latency	0.086	0.168	−0.367**	0.230*
Amplitude	−0.284**	−0.244**	0.362**	−0.263**
CV	0.042	−0.078	0.344**	−0.227*

CV, conduction velocity; HDL, high-density lipoprotein; LDL, low-density lipoprotein. *Significant. **Highly significant.

Table 8 Correlation between lipid profile and sensory nerve conduction

	Cholesterol	Triglycerides	HDL	LDL
Right median nerve				
Latency	0.39*	0.38*	−0.31*	0.20
Amplitude	−0.60**	−0.48**	0.30*	−0.25*
Left median nerve				
Latency	0.51**	0.49**	−0.41*	0.24*
Amplitude	−0.65**	−0.65**	0.40*	−0.27*
Right sural nerve				
Latency	0.47**	0.51**	−0.39*	0.21
Amplitude	−0.61**	−0.60**	0.34*	−0.27*
Left sural nerve				
Latency	0.43**	0.47**	−0.41**	0.26
Amplitude	−0.61**	−0.65**	0.30*	−0.26*

HDL, high-density lipoprotein; LDL, low-density lipoprotein.
*Significant. **Highly significant.

Table 9 Correlation between type of disease severity and type of neuropathy

	Severity				Statistics	
	Mild	Moderate	Severe	Total	*r*	*P*
Type of neuropathy						
Axonal NO (% of severity)	5 (71.4)	6 (17.6)	1 (5.3)	12 (20)	0.307•	0.010
Demyelinating [*n* (% of severity)]	2 (28.6)	7 (20.6)	6 (31.6)	15 (25)		
Mixed [*n* (% of severity)]	0	21 (61.8)	12 (63.2)	33 (55.0)		
Total [*n* (% of severity)]	7 (100.)	34 (100.0)	19 (100)	60 (12)		

Table 10 Correlation between type of disease severity and laboratory findings

	Severity [*n* (%)]				Statistics	
	Mild	Moderate	Severe	Total	*r*	*P*
Group 1	2 (28.6)	14 (41.2)	14 (73.7)	30 (50.0)	0.314*	0.012
Group 2	5 (71.4)	20 (58.8)	5 (26.3)	30 (50.0)		
Total	7 (100.0)	7 (100.0)	34 (100.0)	19 (100.0)		

*Significant.

compared with group 3. Besides, cholesterol and TGs were significantly increased in groups 1 (DM with hyperlipidemia) and 2 when compared with group 3. Moreover, there was a statistically significant increase in abnormal LDL and HDL in group 1 when compared with groups 2 and 3. The study conducted by Goel *et al.* [17] in India on patients with type 2 DM reported that the rate of dyslipidemia was 83%. This percentage reflected the association between diabetes and hyperlipidemia. In addition, results of the present work are comparable to the previous study reporting that type 2 DM is commonly associated with lipid abnormalities such as low plasma HDL cholesterol, high TG and a shift toward smaller and denser LDL particle. Furthermore, clinical evidence suggests that dyslipidemia is associated with the development and progression of DPN [18].

In DM, lipid abnormalities are more widespread because major key enzymes and lipid metabolism pathways are affected owing to the insufficiency of insulin production and secretion [19]. High TGs, low HDL cholesterol, and increased LDL cholesterol are the representative feature of diabetic dyslipidemia [20]. Comparable findings are found in the present work.

In the present work, patients with diabetes and diabetes with dyslipidemia had significantly higher values of HbA1c when compared with the control group. In addition, values of HbA1c were higher in diabetic patients with dyslipidemia when compared with those without dyslipidemia, and this reflects a possible role of dyslipidemia on HbA1c. These results agree with those reported by Sheth *et al.* [21], who reported that patients with dyslipidemia alone or combined with obesity in type 2 DM group have shown poorly controlled HbA1c as compared with those with the normal level of these parameters. Several reports have shown significant influence of lipid concentration on hemoglobin glycation and increased cardiovascular disorder risk, possibly owing to increased insulin resistance [22,23]. Hyperglycemia encourages an increase in LDL glycation and affinity toward LDL receptors on macrophages, which stimulates foam cell formation, endothelial cell toxicity, and smooth muscle proliferation responsible for coronary artery and macrovascular complications [24]. These studies indicated that there is a reciprocal relation (effect) between dyslipidemia and diabetes.

In the present work, we observed a significant association of HDL cholesterol with HbA1c which is in accordance with a study conducted on Nepalese patients with type 2 DM. Moreover, increased dyslipidemia is likely to increase HbA1c and vice versa as the correlation between these parameters are directly proportional and goes hand-in-hand [25]. Reduction in HbA1c in type 2 DM is associated with improved insulin sensitivity and better lipid parameters [21].

In the present work, we found that neurophysiological studies were deranged in patients with DPN when compared with their corresponding controls. These data reflected the association between NCS abnormalities and the development of DPN. Moreover, patients who had dyslipidemia with DPN had more significant abnormalities in NCSs, which were confirmed by a significant correlation between different values of lipid profile and neurophysiological studies.In their study, Asad *et al.* [26] found that

patients with DPN had significant changes in latency, amplitude, and CV when compared with normal controls. These results are comparable to the present work. In addition, they added that both clinical tests and NCS have a value in detecting cases of peripheral neuropathy. The NCS, however, is more powerful in detecting neuropathy, which shows that NCS is helpful also in detecting subclinical neuropathies.

Results of the present study were also in agreement with Song *et al*. [27]; their findings signified that lipid profile was significantly and independently associated with DPN when controlling for confounding factors including age, BMI, glucose profiles, and medical history. They added, in the different indices of lipid profiles, higher levels of the sum of TGs and total cholesterol, as well as TGs and LDL were positively related to the severity of DPN.

Besides, the results of the present work agreed with Yadav *et al*. [28], who reported that the results observed in their study clearly demonstrate the existence of disturbances in lipid metabolism in patients with type 2 DM with peripheral neuropathy.

Conclusion

The results of the present work revealed that the dyslipidemia was added to the hazardous effect of diabetic peripheral neuropathy on neurophysiological studies. Besides, there was a significant correlation between lipid profile and changes in nerve conduction studies. Thus, it is advisable to consider lipid screening in patients with diabetic peripheral neuropathy and the addition of lipid-lowering drugs in those with hyperlipidemia.

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Conflicts of interest

There are no conflicts of interest.

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