



Electrodiagnostic evaluation of median nerve conduction in Type II diabetes mellitus patients that were asymptomatic for peripheral neuropathy: a case control study

Owolabi LF^{1*}, Adebisi S², Danborno B², Buraimoh AA³

¹Department of Medicine, Aminu Kano Teaching Hospital, Bayero University, Kano. ²Department of Human Anatomy, Ahmadu Bello University, Zaria. ³Department of Human Anatomy, Kaduna State University, Kaduna.

*Corresponding author: drlukmanowolabi@yahoo.com

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ABSTRACT

Background: Diabetic neuropathy (DN) is a potentially debilitating complication of diabetes mellitus but many of the diabetic patients are often asymptomatic of DN, thereby, placing them at high risk of developing debilitating complications like diabetic hand and foot. **Aim:** The study was designed to evaluate median nerve conduction of T2DM patients that were asymptomatic for neuropathy and compare their findings with age and sex-matched healthy individuals. **Methods:** The median motor and sensory nerve conduction study was conducted on 100 type 2 diabetic (T2DM) patients and 100 healthy volunteers, matched for age and sex-matched control. Median nerve motor and sensory proximal and Distal latency (DL), Amplitude and Conduction Velocity (CV) as well as motor f-reponse were measured using Nihoen Kohden EMG Machine and standardized techniques of measurement in the course of the study were adhered to. **Results:** On comparison of the median nerve motor and sensory parameters, the median nerve (motor and sensory) distal latencies and f-responses were significantly lower in the control group while the median nerve conduction velocities and amplitudes were significantly higher in the T2DM group. **Conclusion:** The study showed significant impairment of median nerve conduction parameters in T2DM patients who did not have any feature suggestive of peripheral neuropathy when compared with apparently healthy individuals. Thus high index of suspicion as well as early screening for peripheral neuropathy in diabetes is further emphasized.

Key words: Median nerve, diabetic neuropathy, electrodiagnostic evaluation, conduction velocity, latency

INTRODUCTION

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate^[1] so also is the number of diabetic mellitus (DM) patients with diabetic neuropathy (DN) as it is estimated that about 45 % of patients with DM will develop diabetic polyneuropathy (DPN).^[2] If not attended

to, DPN may cause serious complications, such as diabetic ulcers, gangrene, and Charcot joint, with attendant negative effect on the quality of life in diabetic patients.^[3] DN is a frequent microvascular complication of DM, and represents an insidious process for which a disconnection may exist between development of symptoms and signs, and its pathological severity.^[4]



The signs, symptoms, and neurologic deficits in DN vary depending on the classes of nerve fibers involved. Neuropathies may be either sensory or motor^[5,6,7] and may involve primarily small or large nerve fibers.^[8] Diabetic sensorimotor polyneuropathy is the most common clinical subtype seen in clinical practice.^[6,7] It is, potentially, the most debilitating of the complications as many of the patients are often asymptomatic of neuropathy, thus, placing them at high risk of developing devastating hand and foot complications before they present with overt symptoms of diabetic neuropathy.^[9]

In the developed countries, nerve conduction study is widely used for the assessment of DN for detection of the abnormality, evaluate the degree of abnormality and monitoring the clinical course of the disease. Symptoms of DN usually develop at any degree of neuropathic impairment or may not develop at all.^[7] Therefore, there is need to conduct Nerve conduction studies (NCS) whenever DN is suspected as early and precise detection of DN will facilitate early intervention and prevent the crippling complication of DN.

In spite of the rising prevalence of DM and DN in developing countries, there is scarcity of electrodiagnostic facilities necessitating reliance on less specific and less sensitive screening tools like the United Kingdom screening test (UKST) for diagnosis.^[10,11] NCS are more sensitive than clinical examinations as the latter does not offer quantitative results and the NCS are the least variable and non-invasive means of evaluating neuropathy.^[12]

The study was designed to evaluate median nerve conduction in T2DM patients who were asymptomatic for neuropathy and compare their findings with age and sex-matched healthy individuals.

METHODOLOGY

The data was collected over a six-month period at the neuro-diagnostic laboratory of the Aminu Kano Teaching Hospital (AKTH), Bayero University, Kano, Nigeria. One hundred T2DM patients without features suggestive of DN and 100 age and sex-matched control were recruited in the study. The cases were already but recently diagnosed T2DM, on treatment, recruited from the diabetic clinics of the AKTH, Murtala Muhammad Specialist Hospital (MMSH)

and other peripheral hospitals. Diagnosis of DM was made by consultant endocrinologists and senior residents in endocrine and metabolic unit in all cases.

All the participants with features of neuropathy, chronic musculoskeletal disorders, thyroid disorder, leprosy, other chronic systemic disease, alcoholics, smokers and pregnancy were excluded from the study. Neurological examination was done to determine muscle power, stretch reflexes and sensations.

The NCS study was performed with the patients and control lying comfortably in the supine position. A standardized technique was used to obtain and record action potentials for motor and sensory functions.^[13] The protocol adopted in the current study was similar to that used by Kimura^[13] and Hamdan^[14] with minor alteration. The setting for a 4-channel electromyography machine (Nihoen Kohden) machine used in the study was as follows: for median motor nerve conduction, the low cut filter was 2–5 Hz and the high cut was 10 KHz.^[13] Regarding sensory median nerve conduction, low cut was set at 5–10 Hz, high cut was set at 2–3 KHz; the amplification between 20,000 and 100,000 times; electrode impedance was kept below 5 kΩ and the sweep speed for sensory nerve conduction was maintained at 1–2 ms/division while for motor nerve conduction: 2–5 ms/division; and a stimulus duration of 50 μs to 1000 μs and current 0–50 mA are required for effective nerve stimulation.^[13] Supramaximal stimulation (20%–30% more than the current required for maximal action potential) was used.^[13] The NCS evaluation was conducted on their left hands.

Data was collected for proximal and distal latency measured from the onset of action potential, conduction velocity, and amplitude of compound muscle action potential (CMAPA) and sensory nerve action potential (SNAPA) were measured from positive peak to the trough of the action potentials.^[13,14] All the studies were performed with surface recordings and stimulations.

Proximal median nerve stimulation was performed medial to biceps brachii tendon at the elbow crease while the distal median stimulations were performed 10–13 cm proximal to the active surface electrode.^[13]

The Median motor nerve was examined orthodromically. The nerve was stimulated with bipolar surface stimulating electrode at two points along its course.^[13] The action potential was recorded with active and reference surfaces placed close to the motor point of Abductor Policis Brevis and thumb respectively in the case of motor and both electrodes on the first finger in the case of sensory component of the nerve. A ground electrode was placed between the stimulating and recording electrodes.^[13] The motor nerve conduction velocity (MNCV) was calculated using the distance between points of two stimulations by the difference between their latencies.^[13] Sensory nerve conduction was measured antidromically. The sensory nerve conduction velocity (SNCV) was measured by stimulating a single site. Skin surface temperatures were measured over the dorsum of the hand.^[14]

Ethical approval was obtained from the ethical review committee of the Aminu Kano Teaching Hospital Kano. Informed consent was obtained from each participant.

Statistical analysis

All the data generated were collated, checked and analyzed using GraphPad Prism (version 6, GraphPad Software, Inc. CA 92037 USA). Quantitative variables were described using mean with standard deviation and median with range in the case of parametric and non-parametric data respectively. Student t-test and Man Whitney test were used for parametric and non-parametric data respectively for the comparison of nerve conduction parameters between T2DM and control based on normality of the data obtained in various situations. *P*-value of < 0.05 was considered significant.

RESULTS

A total of 100 T2DM patients, who were matched with 100 healthy volunteers by age and sex, comprised fifty eight (58%) males and forty two (42%) females. Their mean age was 49yrs \pm 19 years. The average duration of T2DM was 2.32 \pm 0.83 years.

The median value of median nerve velocities (motor) with their 95% confidence intervals were 47.7m/s (45.8-50.63), 63.9m/s (62.0-63.9) in T2DM and control respectively (*P*<0.0001). The median values of the median nerve distal

latencies (motor) with their 95% confidence interval were 3.2ms (3.1-3.3), 3.0 ms (3.0-3.2) in T2DM and control respectively (*P*=0.0366). The median values of median nerve distal amplitudes (motor) with their 95% confidence interval were 5.5 mv (5.3-6.1), 7.4 mv (7.3-8.1) in T2DM and control respectively (*P*<0.0001). Minimal F-response latencies were 33.7 ms, 95% CI (33.13-35.56) and 27.5, 95% CI (26.4-28.1) respectively (figure 1).

Regarding the sensory component of the median nerve, the median values of median nerve velocities (sensory) with their 95% confidence interval were 32.2m/s (28.0-34.6) and 58.5 m/s (58.2-60.8) in T2DM and control respectively (*P*<0.0001). The median values of the median nerve distal latencies (motor) with their 95% confidence interval were 5.8ms (4.9-5.6) and 2.9 ms (2.8-3.0) in T2DM and control respectively (*P*=0.0366). The mean values of median nerve distal amplitudes (motor) with their 95% confidence interval were 5.7 mv (5.6-6.8) and 7.9 mv (7.5-8.5) in T2DM and control respectively (*P*<0.0001) (figure 2).

DISCUSSION

The current study showed significant impairment of median nerve conduction parameters in T2DM patients without subjective features suggestive of peripheral neuropathy when compared with apparently healthy individuals. The result obtained in our study further corroborated the reports from previous studies that showed median nerve sensorimotor dysfunctions in T2DM patients.^[15-21]

The mechanisms underlying disturbance of nerve conduction in diabetes include metabolic, vascular, autoimmune, and neuro-hormonal growth factor deficiency. Nonetheless, the prevailing theory suggests persistent hyperglycemia as the primary factor of the metabolic hypothesis.^[22] Uncontrolled hyperglycemia increases polyol pathway activity with accumulation of sorbitol and fructose in nerves, damaging them by a yet unknown mechanism.^[22] This is accompanied by decreased myo-inositol uptake and inhibition of the Na⁺/K⁺-adenosine triphosphate with attendant retention of Na⁺, edema, myelin swelling, axo-glial disjunction, and nerve degeneration.^[22,23]

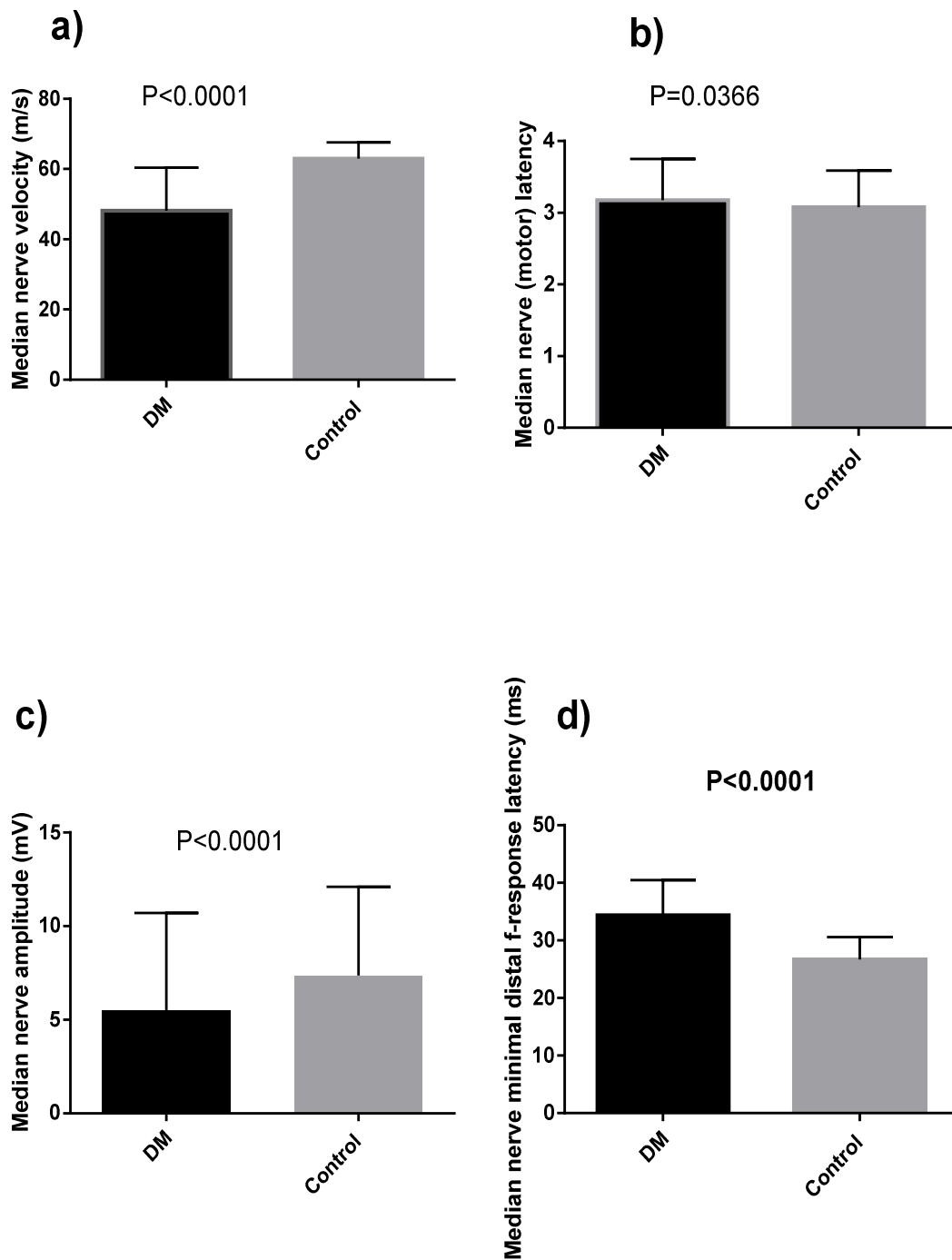


Figure 1: Comparison of median (motor) nerve conduction parameters in DM patients and matched control. It showed significant difference nerve conduction parameters of the median nerve in type-2 DM and matched control (a-d)

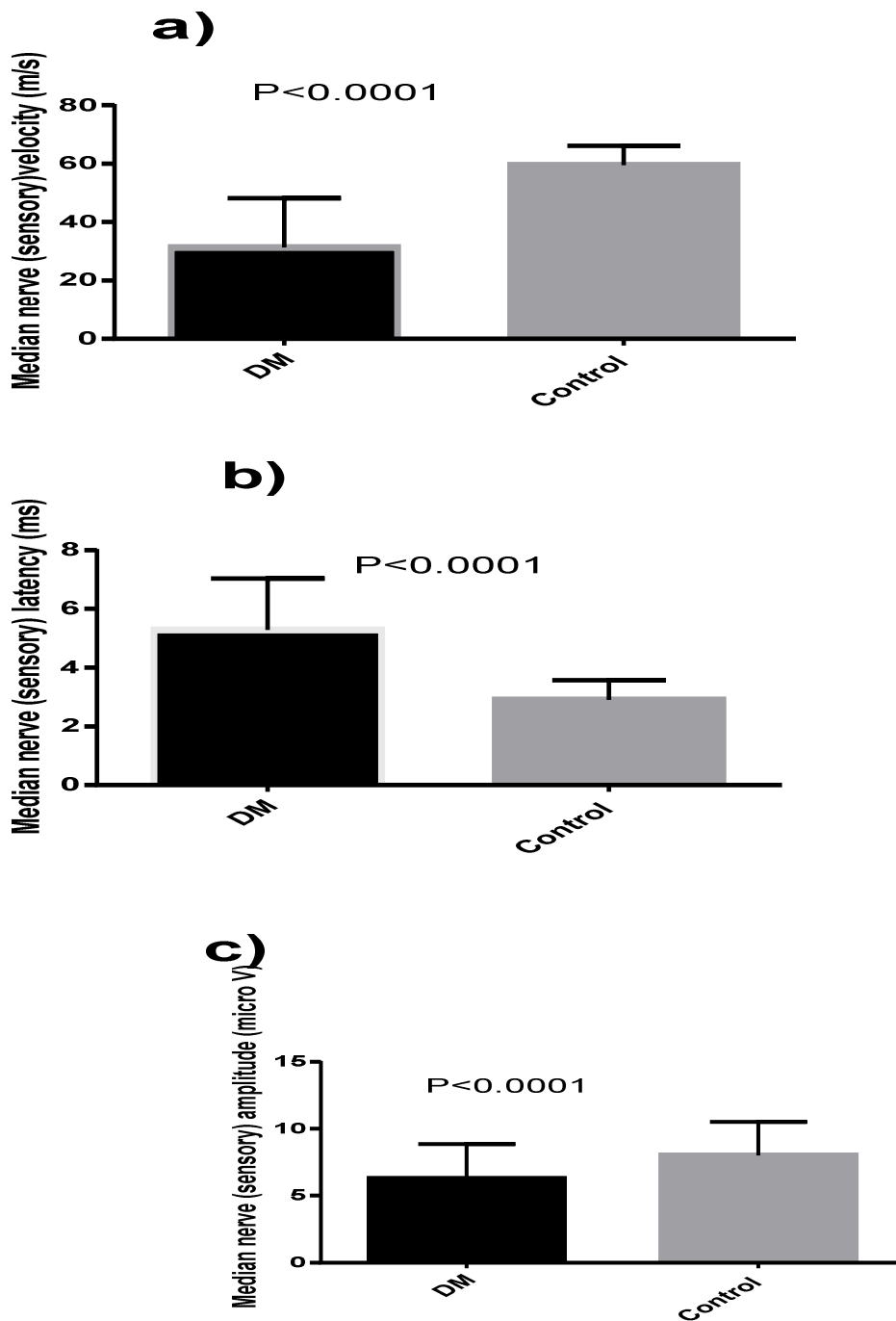


Figure 2: Comparison of median (sensory) nerve conduction parameters in DM patients and matched control. It showed significant difference nerve conduction parameters of the median nerve (sensory) in type-2 DM and matched control (a-c)

Nerve conduction studies are the most objective, accurate, and reliable method for detecting DPN.^[24] DPN is associated with changes in both nerve conduction velocity and amplitude.^[24] Patients with DPN are often asymptomatic and monofilament and vibration perception may appear normal despite substantial nerve fiber degeneration.^[24] Consequently, traditional clinical approaches are, to a large extent, insensitive to subclinical or minimal neuropathy.^[25] It is therefore not uncommon to see some patients present with hand or foot ulcers without a prior diagnosis of DPN.^[26] Thus, patients with DPN may go undiagnosed and opportunities to commence early preventative measures and patient education on proper hand and foot care are missed.^[24]

Our study revealed significant deterioration in motor function in the T2DM group with reduced velocity and amplitude and prolonged distal latency when compared with the control group. This finding is in conformity with the reports of the previous workers.^[27,28] Similarly, the present study showed significant sensory function deterioration evident by reduced velocity and amplitude and prolonged distal latency in the diabetic group in comparison with the control group and the observed difference was much more pronounced in the sensory nerves.

This finding agreed with the notion that DPN may start very early in diabetic patients and that it often involves the sensory fibers initially.^[12,18] However, few studies reported the contrary. Sultana *et al.*^[12] and Biswas^[28] in separate studies reported deterioration of motor nerve function without sensory nerve dysfunction in T2DM. In another study by Bhomwhik,^[29] involving less than 30 newly diagnosed diabetic patients, motor abnormality was predominantly found. The departure of their findings from our observations and those of several other researchers^[15-20] may be explained by the relatively small sample size in their studies.

Reduction in median NCV, which is commonly present even at diagnosis, is one of the earliest neuropathic abnormalities in DM especially in patients with T2DM.^[30,31] In fact, it has been shown that following diagnosis of DM, slowing of median NCV usually progresses at a steady rate by approximately 1 m/s/yr, and that there is positive correlation between the level of impairment and duration of DM.^[31] The early impairment of nerve conduction study

parameters observed in T2DM probably account for the difficulty in terms of restoration of function following intervention late in the disease process. Since sensory fibers are often the first to be affected, for early intervention to be possible and fruitful,^[15] there is a need for high index of suspicion and early nerve conduction measures of sensory function.

In agreement with reports of previous studies,^[15-20] the current study suggests that impairment of nerve conduction may be present in T2DM even in the absence of complaints by the patients and absence of impairment on routine neurological examinations. Although slowing of median NCVs and prolonged distal latencies, which often occurs early in the course of the disorder, are rife in T2DM, the relevance of these abnormalities to the future development of either subclinical manifestations or clinically apparent diabetic neuropathy is still largely uncertain^[23] as NCV does not appear to be related to the severity of symptoms.^[31]

CONCLUSION

To the best of our knowledge, the current study is the first in Nigeria to comparatively assess median nerve conduction status in T2DM using an electromyography machine rather than a questionnaire-based screening instrument. We strongly believe that the findings in the study will contribute to the knowledge-base in respect of median nerve neuropathy in T2DM with the view to emphasizing on early screening, detection and prompt therapeutic intervention in people with or without symptoms of diabetic neuropathy. The study has demonstrated that there is significant impairment of median nerve conduction parameters in T2DM patients without subjective features suggestive of peripheral neuropathy compared with apparently healthy individuals.

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