The usefulness of ultrasonography for the early diagnosis of polyneuropathy in patients with type II diabetes mellitus

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Background: Diabetic neuropathies, affecting over 50% of diabetes patients, present varied forms of polyneuropathy impacting somatic and autonomic nerves. Clinical assessments, laboratory findings, and nerve conduction studies (NCSs) aid in precise diagnosis, while recent technological advances highlight ultrasonography (US) as a promising, cost-effective diagnostic tool. Aims and Objectives: This study aims to assess the efficacy of US in early polyneuropathy diagnosis in type II diabetes, exploring its potential as an alternative to NCS. Materials and Methods: In this prospective observational study, we enrolled 30 adult patients with type II non-controlled diabetes and 30 age-matched controls, comprising 15 controlled diabetic patients and 15 normal individuals. The comprehensive assessments encompassed history-taking for diabetes duration, hypertension, and diabetic complications, along with clinical examinations and investigations involving nerve electrophysiology and US on one upper limb based on patient complaints. Results: Significant increases in the cross-sectional area (CSA) of the median nerve were observed in diabetic peripheral neuropathy groups compared to controls, with a P<0.001. Similarly, at the level behind the medial epicondyle, the ulnar nerve CSA exhibited a significant increase in the diabetic peripheral neuropathy group (11.7 mm²) compared to controls (6.7 mm²) with a P<0.002. In addition, a significant difference in cross-sectional values was found in the median nerve proximal to the carpal tunnel between the two groups (P<0.05). In contrast, no significant differences were observed at other sites. Regarding the relationship between sonography and NCSs, NCSs showed higher sensitivity, but sonography demonstrated comparable specificity in evaluating diabetic peripheral neuropathy. Conclusion: Peripheral nerve US in the upper limb can be a valuable diagnostic tool for identifying and diagnosing diabetic peripheral neuropathy. Key words: Ultrasonography; Diabetic neuropathies; Polyneuropathies; Diabetes mellitus

INTRODUCTION

Diabetic neuropathies stand as prevalent long-term complications in diabetes mellitus (DM), impacting over 50% of patients.¹ Diabetic Polyneuropathy (DPN) manifests in various forms, affecting somatic or autonomic nerves in distal, proximal, large, small, motor, or autonomic nerve fibers. Precise diagnosis of peripheral neuropathies is achievable through clinical assessment, along with laboratory findings and electrophysiological tests.² Nerve conduction studies (NCSs) represent non-invasive, sensitive, and objective procedures. Recent technological advancements have positioned ultrasonography (US) as a promising, cost-effective, reproducible, and comfortable diagnostic tool, offering an alternative approach to detecting neuropathies.³

Despite technological advancements, reports on the utilization of the US for polyneuropathy remain limited.
Existing studies predominantly focus on peripheral nerves in diabetic patients at entrapment sites, such as the median nerve at the carpal tunnel and the tibial nerve at the medial malleolus.  

This study is designed to explore the efficacy of US in the early diagnosis of polyneuropathy among individuals with type II DM. In addition, our objective is to evaluate whether ultrasound can serve as a viable alternative to NCSs in the diagnosis of polyneuropathy in type II diabetic patients.  

Aims and objectives  
This study aims to investigate the utility of ultrasonography in the early detection of polyneuropathy among individuals with type II diabetes mellitus. Additionally, our objective is to evaluate whether ultrasound can serve as a viable alternative to nerve conduction studies for diagnosing polyneuropathy in type II diabetic patients.  

MATERIALS AND METHODS  
This study was approved by the internal review committee of Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. The study was conducted between September 8th, 2023, and January 8th, 2024. Participants obtained written, informed consent.  

Thirty patients with uncontrolled type-2 DM according to the criteria of the Egyptian Diabetes Association were enrolled in our prospective observational study. In addition, we recruited thirty age-matched volunteers, who were divided accordingly into 15 healthy individuals as controls and 15 patients with controlled DM according to the criteria of the Egyptian Diabetes Association. Their ages ranged from 30 to 60 years, for both sexes. Patients were recruited from Nobel Medical College and Teaching Hospital, Biratnagar, Nepal.  

The inclusion criteria for this study encompassed patients with diabetes, both insulin and non-insulin dependent, confirmed through comprehensive clinical evaluations involving systemic and neuromuscular examinations such as light touch, pinprick, position, temperature, vibration senses, knee, and ankle stretch reflexes, along with laboratory tests performed by an internal medicine doctor to ascertain the diagnosis of diabetic peripheral neuropathy (DPN). Subsequently, patients were categorized based on the results as either having or not having DPN. To validate the clinical assessments, NCSs of the upper limbs, indicating sensorimotor polyneuropathy, were conducted using standard procedures and equipment in the electrophysiological department. Exclusion criteria comprised patients with inflammatory disorders, malignancies, alcohol consumption, a history of carpal tunnel operation, complaints of ulnar entrapment, and those exhibiting isolated ulnar nerve entrapment based on electrodiagnostic tests.  

In the clinical assessment phase, a meticulous approach was adopted, involving a comprehensive history-taking process to identify diabetic patients and determine the type of therapy employed, whether oral or insulin therapy. A thorough neurological examination formed the basis for diagnosing peripheral neuropathy, aligning with criteria proposed by England et al., and the American Academy of Neurology. Patients undergoing examination exhibited symmetrically reduced or absent ankle reflexes, decreased vibration perception by a 128 Hz tuning fork, and diminished distal sensation. The NCSs phase involved motor and sensory testing using surface recording electrodes with standard placement. Motor NCSs for the median and ulnar nerves assessed compound muscle action potentials, while sensory NCSs evaluated nerve conduction velocities for both nerves. Electrophysiological diagnoses of diabetic peripheral neuropathy (DPN) were determined based on established normative values, excluding patients with other neuropathic findings. Classification into four groups ensued: normal, Carpal Tunnel Syndrome (CTS), DPN, or DPN with concurrent CTS (DPN+CTS).  

The subsequent phase involved an ultrasonographic examination conducted by a radiology specialist using a 6–18 MHz linear array probe. Participants were positioned supinely on the examination table and median and ulnar nerve cross-sectional areas (CSAs) were measured at three levels. For the median nerve, measurements were taken proximal to the carpal tunnel, at the carpal tunnel, and distal to it, while ulnar nerve CSAs was measured at the medial epicondyle. The transducer was applied perpendicularly to

### Table 1: CSA values of the median nerve of the control group and DPN patients at different sites

<table>
<thead>
<tr>
<th>Median nerve at different sites</th>
<th>Control (n=15)</th>
<th>Diabetic (n=45)</th>
<th>P-value (paired sample t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Minimum</td>
</tr>
<tr>
<td>MNPCT (mm²)</td>
<td>8</td>
<td>1.53</td>
<td>6</td>
</tr>
<tr>
<td>MACT (mm²)</td>
<td>8</td>
<td>1.53</td>
<td>6</td>
</tr>
<tr>
<td>MNDCT (mm²)</td>
<td>8</td>
<td>1.53</td>
<td>6</td>
</tr>
</tbody>
</table>

MNPT: Median nerve proximal to the carpal tunnel. MACT: Median nerve at the carpal tunnel. MNDCT: Median nerve distal to the carpal tunnel. CSA: Cross-sectional area.
the nerves on the skin without additional pressure. CSAs were measured by tracing the nerve just inside its hyperechoic rim, and the average value was used for each level. A CSA >10 mm² at the pisiform level served as the sonographic diagnostic threshold for CTS, per the literature.\(^6\)

The data were coded and entered using the Statistical Package for the Social Sciences (SPSS) version 15. Descriptive statistics, encompassing mean, standard deviation, median, and interquartile range for quantitative variables, as well as number and percentage for qualitative values, were utilized to summarize the data. Statistical differences between groups were assessed employing the Chi-square test for qualitative variables. In addition, non-parametric tests such as the Mann–Whitney test and the Kruskal–Wallis test were employed for quantitative variables that did not adhere to a normal distribution. Results with P-values equal to or <0.05 were considered statistically significant.

**RESULTS**

A total of 60 patients between the age groups of 30 and 60 years were analyzed in this study after fulfilling the inclusion and exclusion criteria. Patients were divided into two groups. The first group was of 30 patients with uncontrolled type II DM, and the second group was of 15 patients with controlled type II DM and 15 normal individuals. Females constitute 60%. The mean age of the patients was 51 years.

Out of 45 patients diagnosed with type II DM, 57.7% were on insulin and 42.3% were on oral hypoglycemic drugs. For analysis, the patient was again divided into groups A (insulin-dependent) and B (insulin-independent).

Table 1 shows there is a very high statistical significance increase in the median nerve CSA in the DPN groups when compared with the control group, with a P<0.001.

Behind the medial epicondyle level, the ulnar nerve CSA shows a statistically significant increase in the DPN group (11.7 mm²) in comparison to the control groups (6.7 mm²) with a P<0.002 as shown in Table 2.

Table 3 shows that there is a statistically significant difference between the CSA values obtained from the median nerve proximal to the carpal tunnel between Group A and Group B with a P<0.05. Otherwise, there is no statistically significant difference between the values obtained from the rest of the sites compared to the two groups.

Table 4 shows the nerve mean measurement variations while comparing the distal to proximal nerve segments between non-entrapment and entrapment sites of the nerves along their course. The nerves showed diffuse nerve enlargement at the entrapment sites.

Moreover, the nerves were smaller distally than proximally at non-entrapment sites but not at entrapment sites. The proximal to distal difference in CSA was greater in DPN than in controls for the ulnar nerve, and it showed a trend toward a difference in the median nerve.

Table 5 shows the relationship between sonography and NC by comparing the sensitivity and specificity of both modalities. Sensitivity was higher for NCS than sonography in the evaluation of DPN. However, sonographic specificity approaches that of the NCS results.
DISCUSSION

Distal symmetrical sensorimotor polyneuropathy is a prevailing complication in individuals with type II DM, contributing to severe complications such as diabetic foot ulcers, gangrene, Charcot joint, and flexion contractures, ultimately diminishing the patient’s quality of life. The conventional diagnostic approach involves clinical examination and confirmation through sensory and motor NCSs. Although NCS is reliable, it is time-consuming, mildly invasive, and less tolerable for repeated assessments. Furthermore, NCS primarily assesses large nerve fibers, while small fibers, often the first to be affected in diabetic polyneuropathy (DPN), are not adequately addressed.

In contrast, sonographic examinations offer a non-invasive and more comfortable technique for dynamically evaluating nerve structures, making them suitable for assessing peripheral nervous system disorders, including CTS and DPN. This study aimed to assess whether sonographic findings in the median and ulnar nerves corresponded to clinical data and results from motor and sensory NCS. The study revealed a statistically significant increase in CSA of both median and ulnar nerves in type II non-controlled diabetic patients with sensory manifestations and positive NCS compared to control groups. Moreover, the study indicates a potential role for nerve CSA values in gauging the severity of diabetic polyneuropathy. Both NCS and US examinations hold significance in the diagnostic process of diabetic polyneuropathy. NCS provides insights into nerve function, aiding in differential diagnosis, while US sonography offers a non-invasive and more comfortable approach for patients, enabling dynamic and detailed evaluation of nerve structures.

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REFERENCES


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