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"A Study Of High-Resolution Ultrasound Of Pheripheral Nerves (Ulnar, Median, Common Peroneal And Tibial) In Diabetic Neuropathy And Its Correlation With Nerve Conduction Study"

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Abstract
Background: *Diabetic neuropathy is a prevalent complication of both type 1 and type 2 diabetes mellitus (DM). Diabetic peripheral neuropathy (DPN) affects approximately 30% of those with diabetes, primarily impacting the feet and legs, though it can also involve the arms and hands. Neuropathic pain in DPN can affect up to 30% of patients, significantly impairing quality of life, increasing dependence on medication, and correlating with higher morbidity and mortality rates.*
Aims and Objective: *To assess the cross-sectional area (CSA) of specific peripheral nerves—namely, the median nerve at the wrist, ulnar nerve at the elbow, tibial nerve at the ankle, and common peroneal nerve at the knee—in individuals suspected of having DPN. Additionally, it sought to investigate the correlation between CSA measurements and nerve conduction studies (NCS), as well as to explore patterns of nerve involvement and morphological changes in these peripheral nerves.*
Material and Methods:*This cross-sectional observational study was conducted at C.S.S. Hospital, affiliated with S.V.S.U., from February 2023 to August 2024, with approval from the Institutional Ethics Committee. Data were gathered from 70 patients exhibiting symptoms of neuropathy, including both outpatient and inpatient cases. High-resolution ultrasound and Nerve conduction study (NCV) of peripheral nerves was performed on patients diagnosed with Type 2 Diabetes Mellitus (T2DM), based on clinical symptoms and HbA1c levels.*
Conclusion: *Our study demonstrated a positive correlation between increased cross-sectional areas (CSA) of peripheral nerves and abnormalities in nerve conduction studies (NCS). Ultrasound (US) effectively detected morphological changes in nerves before electrodiagnostic issues, indicating its potential for early DPN detection. DPN patients had significantly higher CSA values than those without the condition.We observed distinct NCS patterns: lower limb nerves typically showed axonopathy, while upper limb nerves exhibited more demyelination, underscoring the greater impact on lower limbs in DPN.*

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I. Introduction

Diabetic neuropathy is a prevalent complication of both type 1 and type 2 diabetes mellitus (DM), currently affecting around 8.4 million individuals worldwide, with projections indicating this number could rise to over 13 million by 2040.[1] DM is characterized by insufficient insulin production or cellular resistance to insulin, resulting in uncontrolled blood sugar levels that can damage nerves and blood vessels.[2,3]

Diabetic peripheral neuropathy (DPN) affects approximately 30% of those with diabetes, primarily impacting the feet and legs, though it can also involve the arms and hands. Symptoms include numbness, tingling, and sharp or burning pain, often presenting asymmetrically. Neuropathic pain in DPN can affect up to 30% of patients, significantly impairing quality of life, increasing dependence on medication, and correlating with higher morbidity and mortality rates.[4-8]

DPN can manifest in various forms, with symmetric sensory-motor axonal neuropathy being the most common. The exact causes remain unclear but may involve metabolic, neurovascular, autoimmune processes, and lifestyle factors. Diagnosis typically includes clinical assessments, the Toronto Clinical Neuropathy Score (TCNS), and laboratory tests, with high-resolution ultrasonography (HRU) increasingly used for detailed nerve evaluations.[9-18]

This study aimed to assess the cross-sectional area (CSA) of specific peripheral nerves—namely, the median nerve at the wrist, ulnar nerve at the elbow, tibial nerve at the ankle, and common peroneal nerve at the knee—in individuals suspected of having DPN. Additionally, it sought to investigate the correlation between CSA measurements and nerve conduction studies (NCS), as well as to explore patterns of nerve involvement and morphological changes in these peripheral nerves.

Pathophysiology: Diabetes primarily affects the peripheral nervous system (PNS), making long axons particularly vulnerable to damage. Sensory neurons, especially small unmyelinated C-fibers responsible for transmitting pain and heat sensations, are especially at risk. The progression of DPN leads to degeneration of C-fibers, followed by demyelination of larger fibers and eventual axonal loss, typically resulting in numbness and reduced proprioception that follows a distal-to-proximal pattern.[19,20]

Morphological Changes in Nerve: High-resolution ultrasonography (HRU) is vital for assessing morphological changes in nerve tissues and diagnosing diabetic peripheral neuropathy (DPN). It evaluates nerve size, vascularity, echogenicity, and mobility, revealing key structural insights. In diabetic patients, a notable change is the enlargement of the nerve cross-sectional area (CSA), often accompanied by a loss of the typical "honeycomb structure." Both longitudinal and transverse nerve diameters increase, and echogenicity decrease and boundary fuzziness are significantly higher than in non-diabetic controls, indicating structural alterations associated with diabetic neuropathy.[21-26]

II. Materials And Methods:

This cross-sectional observational study was conducted at C.S.S. Hospital, affiliated with S.V.S.U., from February 2023 to August 2024, with approval from the Institutional Ethics Committee. Data were gathered from 70 patients exhibiting symptoms of neuropathy, including both outpatient and inpatient cases. High-resolution ultrasound of peripheral nerves was performed on patients diagnosed with Type 2 Diabetes Mellitus (T2DM), based on clinical symptoms and HbA1c levels, using the Samsung HS50 and HS70 ultrasound machines.

The study excluded individuals with Type 1 or secondary diabetes accompanied by end-organ failure affecting nerve function, those on medications known to induce neuropathy, patients with thyroid disease, a history of severe limb trauma, individuals under 18 years of age, pregnant or lactating women, and those with other forms of neuropathy (such as inflammatory, hereditary, or metabolic).

Scanning Technique: Cross-sectional areas (CSAs) of peripheral nerves were measured by tracing their hyperechoic rims, taking three measurements for accuracy. Color Doppler mode was used to exclude blood vessels, and the transducer was applied with minimal pressure. Measurements were taken for the median nerve proximal to the carpal tunnel, the ulnar nerve at the cubital tunnel, the tibial nerve behind the medial malleolus, and the common peroneal nerve at the fibular head in both limbs.[21]

Electrodiagnostic Examination (EDX)

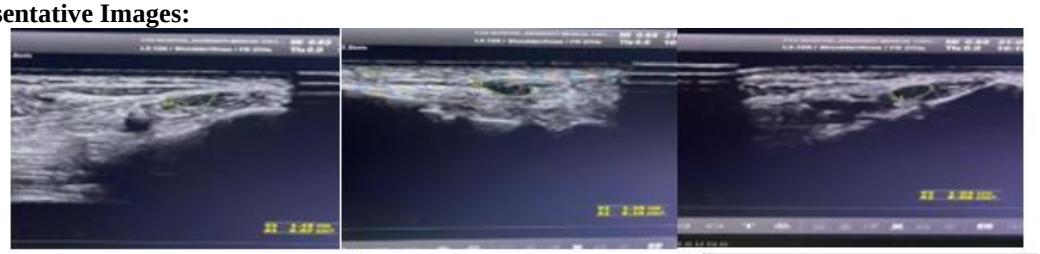
Bilateral nerve conduction studies (NCS) were conducted on the median, ulnar, tibial, and common peroneal nerves in both limbs, using a NEUROWERK diagnostic device in a controlled environment. Participants were asked to remove cosmetics to improve electrical contact.

For tibial nerve assessment, participants lay prone, with electrodes placed near the navicular tubercle and medial malleolus for distal stimulation, and at the popliteal fossa for proximal stimulation. In common peroneal nerve studies, participants lay supine, with electrodes on the extensor digitorum brevis and stimulation near the tibialis anterior tendon and below the fibular head. An accessory deep peroneal nerve was evaluated if the proximal amplitude exceeded the distal.[27]

For median nerve sensory studies, electrodes were placed at the wrist and index finger, while for ulnar sensory studies, electrodes were positioned at the wrist and little finger.[28] Motor conduction studies assessed

onset latency, peak amplitudes, spike area, and duration, with nerve conduction velocity (NCV) calculated from distance and latency differences. Sensory studies included measurements of onset latency and peak amplitudes.[29]

Representative Images:



(A) Posterior tibial nerve in a patient with DPN at medial malleolus with CSA 0.07 cm2 or 7.0 mm2.

(B) Common peroneal nerve at the neck of fibula with CSA 0.10 cm2 or 10.0 mm2 in a patient with DPN.

(C) Posterior tibial nerve in a patient with DPN at medial malleolus with CSA 0.08 cm2 or 8.0 mm2 and shows decrease in

III. Result

Our study found a mean age of 52.06 years (range 23–79) among participants, with illness duration since diagnosis ranging from 2 to 40 years and a mean duration of 21.04 ± 8.23 years. Glycated hemoglobin (HbA1c) levels varied from 5.6 to 14.3%, averaging 9.03 ± 2.5%. Table 1 presents the mean cross-sectional area (CSA) of the right upper and lower limb nerves, including the median nerve at the wrist, ulnar nerve at the elbow, tibial nerve at the ankle, and common peroneal nerve at the knee.

Table 1: Cross Sectional Area (mm2) of Bilateral Limbs Median, Ulnar, Tibial and Common Peroneal Nerves

Variables	N	Minimum	Maximum	Mean	Std. Deviation	Median	Q1	Q3
Median Nerve Right (mm^2)	70	8.5	13.9	10.484	1.35	10.45	9.30	11.42
Ulnar Nerve Right (mm^2)	70	7.8	13.6	9.891	1.70	9.20	8.67	10.90
Tibial Nerve Right (mm^2)	70	5.9	9.8	7.556	0.97	7.50	6.87	8.20
CPN Right (mm^2)	70	7.8	15.9	11.107	2.13	10.85	9.37	12.72
Median nerve Left (mm^2)	70	8.4	14.1	10.497	1.56	9.90	9.00	11.62
Ulnar nerve Left (mm^2)	70	7.8	13.8	9.944	1.62	9.80	8.57	11.15
Tibial nerve Left (mm^2)	70	5.6	10.0	7.567	1.00	7.40	6.70	8.22
CPN Left (mm^2)	70	6.7	15.6	10.756	2.10	10.70	8.97	11.90

Table 2: Nerve wise correlation between diabetic neuropathy and USG measured cross-sectional area (mm^2) right side of the cases

Variables	Group	N	Mean Of CSA (mm^2)	Std. Deviation	T value	P value
Median Nerve Right (mm^2)	**Diabetic without neuropathy**	36	10.17	1.30	-2.029	0.046*
	Diabetic neuropathy	34	10.82	1.35		
Ulnar Nerve Right (mm^2)	**Diabetic without neuropathy**	36	9.42	1.49	-2.481	0.016*
	Diabetic neuropathy	34	10.39	1.78		
Tibial nerve Right (mm^2)	**Diabetic without neuropathy**	36	7.09	0.83	-4.694	0.000*
	Diabetic neuropathy	34	8.04	0.87		
CPN Right (mm^2)	**Diabetic without neuropathy**	36	10.09	1.79	-4.672	0.000*
	Diabetic neuropathy	34	12.18	1.94		

*Significant at 5% level of significance

Table 3: Nerve wise correlation between diabetic neuropathy and USG measured cross-sectional area (mm^2) left side of the cases

Variables	Group	N	Mean Of CSA (mm^2)	Std. Deviation	T value	P value
Median nerve Left (mm^2)	**Diabetic without neuropathy**	36	10.18	1.43	-1.787	0.078

	Diabetic neuropathy	34	10.84	1.65		
Ulnar nerve Left (mm^2)	**Diabetic without neuropathy**	36	9.38	1.39	-3.232	0.002*
	Diabetic neuropathy	34	10.55	1.64		
Tibial nerve Left (mm^2)	**Diabetic without neuropathy**	36	7.14	0.84	-4.071	0.000*
	Diabetic neuropathy	34	8.02	0.97		
CPN Left (mm^2)	**Diabetic without neuropathy**	36	9.75	1.72	-4.703	0.000*
	Diabetic neuropathy	34	11.82	1.96		

*Significant at 5% level of significance

Table 4: Nerve wise correlation between NCS pattern and USG measured cross-sectional area right side of the cases

Right side Cross-sectional area Nerve	Normal NCS				Axonal				Demyelinating				Not recordable				F Value	P value
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max		
Median Nerve	10.5	1.4	8.5	13.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ulnar Nerve	9.8	1.7	7.8	13.6	-	.	-	-	12.8	.	12.8	12.8	-	-	-	-	1.616	0.206
Tibial Nerve	7.4	.9	5.9	9.8	7.3	.6	6.7	8.2	-	-	-	-	8.5	.6	7.6	9.4	9.166	0.000*
CPN	10.2	1.8	7.8	14.7	11.9	2.0	8.6	15.9	-	-	-	-	13.2	1.5	10.3	15.0	16.826	0.000*

*Significant at 5% level of significance

Table 5: Nerve wise correlation between NCS pattern and USG measured cross-sectional area left side of the cases

Left side Cross-sectional area Nerve	Normal NCS				Axonal				Demyelinating				Not recordable				F Value	P value
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max		
Median Nerve	10.5	1.6	8.4	14.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ulnar Nerve	9.9	1.6	7.8	13.8	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tibial Nerve	7.3	1.0	5.6	9.9	7.8	1.0	6.9	10.0	-	-	-	-	8.4	.8	6.8	9.6	6.044	0.004*
CPN	9.9	1.8	6.7	14.7	10.9	1.6	8.3	13.3	15.6	-	15.6	15.6	13.0	1.4	11.3	15.5	13.873	0.000*

*Significant at 5% level of significance

In our study, all diabetic patients had normal nerve conduction study (NCS) results for the median nerve, with a mean cross-sectional area (CSA) of 10.5 ± 1.4 mm^2 at the wrist for those without diabetic peripheral neuropathy (DPN). For the ulnar nerve, 98.5% had normal NCS results, while 1.42% showed a demyelinating pattern; the CSA at the elbow was 9.8 ± 1.7 mm^2 on the right and 9.9 ± 1.6 mm^2 on the left for patients without DPN, and 12.8 mm^2 on the right for those with DPN, with no neuropathy detected on the left.

For the tibial nerve, 75.7% had normal NCS results, 10% exhibited an axonal pattern, and 15.7% had non-recordable results. The CSA at the ankle was 7.09 ± 0.83 mm^2 on the right and 7.14 ± 0.84 mm^2 on the left for patients without DPN, compared to 8.04 ± 0.87 mm^2 bilaterally for those with DPN.

In the common peroneal nerve, 60% had normal NCS results, 18.5% showed an axonal pattern, 1.42% had a demyelinating pattern, and 20% had non-recordable results. The CSA at the knee for patients without DPN was 10.09 ± 1.79 mm^2 on the right and 9.75 ± 1.72 mm^2 on the left, while for those with DPN, it was 12.18 ± 1.94 mm^2 on the right and 11.82 ± 1.96 mm^2 on the left.

IV. Discussion

Our study included 70 diabetic patients suspected of having diabetic peripheral neuropathy (DPN) found a significant correlation between HbA1c levels and nerve cross-sectional area (CSA) ($p < 0.05$), consistent with Tanu Ranjan et al. and Watanabe et al., but differing from Riazi et al. and Kelle et al.[3,16,30,31]

In our ultrasonography assessments of diabetic neuropathy patients, we observed significant nerve changes, including increased cross-sectional area (CSA), loss of the honeycomb pattern, blurred margins, and heightened echogenicity. These alterations are characteristic of diabetic peripheral neuropathy (DPN) and are associated with oxidative stress from microangiopathy and sorbitol buildup in Schwann cells, resulting in axonal damage and demyelination. Similar findings have been reported by Shamrendra Narayan et al., Singh et al., and Ishibashi et al.[21,26,32]

In our study, we measured the mean cross-sectional area (CSA) values for nerves as follows: 10.48 ± 1.35 mm^2 for the median nerve, 9.89 ± 1.70 mm^2 for the ulnar nerve, 7.55 ± 0.97 mm^2 for the tibial nerve, and

11.10 ± 2.13 mm² for the common peroneal nerve, with identical values on both sides. While our findings align with other studies for upper limb nerves, we observed lower CSA values for the tibial and common peroneal nerves, possibly due to demographic differences. Notably, Tsuneo Watanabe et al. reported higher CSAs for the median and tibial nerves in diabetic patients, while Shamrendra Narayan et al. and Seok Kang et al. found larger CSAs across various nerves.[16,21,33]

Nerve conduction studies (NCS) categorized patients into axonal, demyelinating, mixed, and non-recordable groups, with those having normal NCS patterns showing significantly lower CSA values.

We found that lower limb nerves primarily exhibited axonopathy, while upper limb nerves showed more demyelination, aligning with findings by Narayan S. et al.[21] In DPN cases, 10% of tibial and 18.5% of common peroneal nerves exhibited axonopathy, with only 1.42% of lower limb nerves showing primary demyelination.

The increased CSA in demyelinating neuropathies indicates thicker nerves, emphasizing NCS's role in differentiating neuropathy types. In advanced cases where NCS may be non-recordable, CSA measurements were higher, reinforcing that diabetic neuropathy initially affects lower limbs before upper limbs, as noted by Narayan S. et al. and Callaghan et al.[21,34]

V. Conclusion

Our study demonstrated a positive correlation between increased cross-sectional areas (CSA) of peripheral nerves and abnormalities in nerve conduction studies (NCS). Ultrasound (US) effectively detected morphological changes in nerves before electrodiagnostic issues, indicating its potential for early DPN detection. DPN patients had significantly higher CSA values than those without the condition. We observed distinct NCS patterns: lower limb nerves typically showed axonopathy, while upper limb nerves exhibited more demyelination, underscoring the greater impact on lower limbs in DPN.

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