"High-Resolution Ultrasound Analysis of Tibial Nerve Cross-Sectional area in Diabetic Neuropathy"

Dr. Somya Nath Banerjee[1], **Dr. M. Kalaichezhian**[1*], **Prof. Dr. Murugan Gopalakrishnan**[1]

[1*]Department of Radiology, Sree Balaji Medical College and Hospital, Chrompet, Chennai - 600044, Tamil Nadu, India

[1]Junior Resident (Dr. Somya Nath Banerjee) | Email: empsomy@gmail.com

[1]Professor (Dr. M. Kalaichezhian) | ORCID: https://orcid.org/0000-0002-2857-5477 | Email: sonomedscans@gmail.com

[1]Professor & HOD (Prof. Dr. Murugan Gopalakrishnan) | ORCID: https://orcid.org/0000-0003-2943-8666 | Email: dr.gmurugan@yahoo.com

***Corresponding Author:** Dr. M. Kalaichezhian, Professor, Department of Radiology, Sree Balaji Medical College and Hospital, Chrompet, Chennai - 600044, Tamil Nadu, India | ORCID: https://orcid.org/0000-0002-2857-5477 | Email: sonomedscans@gmail.com

ABSTRACT

Background

Diabetic peripheral neuropathy is one of the most common chronic complications of diabetes mellitus and is a major contributor to foot ulcers, disability, and reduced quality of life. Conventional diagnostic methods primarily assess functional impairment and may not adequately reflect underlying structural nerve changes. High-resolution ultrasonography enables direct visualization of peripheral nerve morphology and measurement of nerve cross-sectional area, offering a non-invasive method to assess structural involvement. Evaluation of the tibial nerve is particularly relevant due to its length-dependent involvement in diabetic neuropathy.

Objectives

To evaluate the cross-sectional area of the tibial nerve using high-resolution ultrasonography in patients with diabetic peripheral neuropathy and to assess its association with neuropathy severity, duration of diabetes, and glycaemic control.

Materials and Methods

This hospital-based observational study was conducted in the Department of Radiodiagnosis and Imaging at a tertiary care center in Chennai over a period of nineteen months. A total of 77 adult patients with type 2 diabetes mellitus and clinically as well as electrophysiologically confirmed diabetic peripheral neuropathy were included. High-resolution ultrasound was used to measure tibial nerve cross-sectional area at the level of the medial malleolus using a standardized protocol. Neuropathy severity was graded using the Toronto Clinical Neuropathy Score. Associations between tibial nerve cross-sectional area and neuropathy severity, duration of diabetes, and HbA1c were analyzed using appropriate statistical tests.

Results

The mean tibial nerve cross-sectional area was increased bilaterally, measuring 13.8 ± 2.4 mm² on the right and 13.6 ± 2.3 mm² on the left, with no significant side-to-side difference. Tibial nerve cross-sectional area increased progressively with neuropathy severity, from 11.6 ± 1.3 mm² in mild neuropathy to 16.2 ± 1.9 mm² in severe neuropathy ($p < 0.001$). A strong positive correlation was observed between tibial nerve cross-sectional area and Toronto Clinical Neuropathy Score ($r = 0.71$, $p < 0.001$). Cross-sectional area also showed significant positive correlations with duration of diabetes ($r = 0.64$, $p < 0.001$) and HbA1c levels. Multivariate analysis identified neuropathy severity, duration of diabetes, and glycaemic control as independent predictors of tibial nerve enlargement. A cross-sectional area cut-off value of >12 mm² demonstrated good diagnostic performance.

Conclusion

High-resolution ultrasonography demonstrates significant structural enlargement of the tibial nerve in patients with diabetic peripheral neuropathy. Tibial nerve cross-sectional area correlates strongly with neuropathy severity, duration of diabetes, and glycaemic control, indicating its potential role as a reliable structural marker of diabetic neuropathy. Ultrasonographic assessment of the tibial nerve may serve as a useful adjunct to clinical and electrophysiological evaluation in routine practice.

Keywords

Diabetic peripheral neuropathy; Tibial nerve; High-resolution ultrasonography; Cross-sectional area; Diabetes mellitus

How to cite this article: Banerjee SN, Kalaichezhian M, Gopalakrishnan M. High-Resolution Ultrasound Analysis of Tibial Nerve Cross-Sectional area in Diabetic Neuropathy. Int J Drug Deliv Technol. 2026;16(71s): 507-515. DOI: 10.25258/ijddt.16.71s.62

INTRODUCTION

Diabetic neuropathy represents a heterogeneous group of nerve disorders that occur as a direct consequence of diabetes mellitus and is recognized as a frequent and disabling chronic complication. According to standard neurology and endocrinology texts, diabetic neuropathy is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in individuals with diabetes after exclusion of other causes of neuropathy [1]. The American Diabetes Association further describes diabetic neuropathy as a spectrum of clinical and subclinical syndromes affecting sensory, motor, and autonomic nerves, with distal symmetric polyneuropathy being the most common form [2]. From an imaging and anatomical perspective, peripheral nerves consist of organized fascicles surrounded by epineurium, perineurium, and endoneurium, structures that can be visualized using high-resolution sonographic techniques when appropriate transducers and protocols are employed [3]. Musculoskeletal and neuromuscular ultrasound textbooks emphasize that normal peripheral nerves exhibit a characteristic honeycomb appearance on transverse imaging, with consistent cross-sectional area values that vary according to anatomical location [4]. Any deviation from these normative measurements may indicate underlying pathological processes, including metabolic neuropathies such as those related to diabetes [5].

The pathophysiology of diabetic neuropathy is multifactorial and involves chronic hyperglycemia-induced metabolic and microvascular injury to peripheral nerves. The American Diabetes Association position statement highlights mechanisms including polyol pathway activation, oxidative stress, advanced glycation end-product formation, impaired axonal transport, and endoneurial ischemia, all of which contribute to progressive nerve fiber damage [6]. From a global perspective, the burden of diabetes itself has reached alarming proportions, with the International Diabetes Federation reporting hundreds of millions of individuals affected worldwide and a steady increase projected over the coming decades [7]. As the duration of diabetes lengthens and glycemic control remains suboptimal in large populations, the prevalence of diabetic neuropathy correspondingly rises, making it a major contributor to morbidity, disability, and health-care expenditure globally [8].

Diabetic peripheral neuropathy has particular clinical importance because of its strong association with lower-limb complications. The neuropathic process predominantly affects distal nerves of the lower extremities, resulting in loss of protective sensation, altered proprioception, and motor imbalance. This cascade significantly increases the risk of foot ulceration, infection, and eventual lower-limb amputation [9]. Clinical studies have demonstrated that neuropathy is a key initiating factor in the pathway leading to diabetic foot disease, accounting for a substantial proportion of non-traumatic amputations worldwide [10]. In addition to physical disability, diabetic neuropathy is associated with chronic pain syndromes, sleep disturbances, psychological stress, and reduced quality of life, underscoring the need for early detection and effective monitoring strategies [11].

Recent advances in neurobiology have expanded the understanding of diabetic neuropathy beyond a purely functional disorder, emphasizing structural and bioenergetic alterations within peripheral nerves. Experimental and clinical research has shown that axonal swelling, demyelination, and fascicular enlargement may occur as part of the neuropathic process, particularly in long-standing diabetes [12]. Clinically, diabetic neuropathy presents with a wide range of manifestations, from asymptomatic nerve dysfunction to severe sensory loss and debilitating neuropathic pain, which often remain underdiagnosed in routine practice [13]. Consensus-based diagnostic criteria proposed by expert panels stress the importance of combining clinical findings with objective assessments to improve diagnostic accuracy and disease stratification [14].

Epidemiological studies indicate that the prevalence of diabetic polyneuropathy varies widely depending on population characteristics, diagnostic methods, and disease duration. Large observational studies have consistently demonstrated that neuropathy is not limited to overt diabetes but may also be present in individuals with impaired glucose tolerance and prediabetes, suggesting that nerve damage may begin early in the metabolic disease continuum [15].

The global diabetes epidemic is mirrored by rising rates of diabetic neuropathy, making it a significant public health challenge. The most recent International Diabetes Federation Atlas confirms a continued upward trend in diabetes prevalence, especially in low- and middle-income countries, where access to early diagnostic tools remains limited [16].

India represents one of the epicenters of the global diabetes burden. Epidemiological data indicate that India harbors one of the largest populations of individuals with diabetes, with substantial regional variation influenced by urbanization, lifestyle changes, and socioeconomic factors [17]. Population-based studies conducted across multiple Indian states have demonstrated high prevalence rates of both diabetes and prediabetes, highlighting the magnitude of the problem at a national level [18].

In southern India, including Tamil Nadu, the burden of diabetes-related complications is particularly pronounced, with diabetic neuropathy contributing significantly to foot complications and associated health-care costs [19]. Longitudinal observations suggest that as diabetes prevalence increases and patients survive longer due to improved medical

care, the incidence and severity of neuropathic complications are likely to rise further, emphasizing the need for scalable and accessible diagnostic modalities [20].

Despite its clinical significance, diabetic neuropathy often remains underdiagnosed, especially in its early stages. Conventional diagnostic tools such as nerve conduction studies and electromyography primarily assess large myelinated fibers and may fail to detect early or small-fiber neuropathy. Furthermore, these tests are time-consuming, invasive, and not always feasible for routine screening in high-volume clinical settings. High-resolution ultrasound has emerged as a promising non-invasive imaging modality capable of visualizing peripheral nerve morphology in real time.

The tibial nerve is of particular interest in diabetic neuropathy due to its anatomical location, length, and vulnerability to metabolic and ischemic injury. Enlargement of nerve cross-sectional area has been proposed as an imaging biomarker of neuropathic involvement, reflecting axonal edema, demyelination, and connective tissue proliferation. High-resolution ultrasound offers advantages of wide availability, absence of radiation, cost-effectiveness, and suitability for repeated follow-up examinations, making it an attractive tool for both clinical practice and research.Therefore, this study was undertaken to evaluate tibial nerve cross-sectional area using high-resolution ultrasound in diabetic neuropathy patients and to explore its correlation with clinical manifestations of neuropathy.

METHODOLOGY

Study Design

The present study was conducted as an observational hospital-based study designed to evaluate the cross-sectional area of the tibial nerve using high-resolution ultrasonography in patients with diabetic peripheral neuropathy. The study focused on structural nerve assessment without any interventional component.

Study Setting and Study Period

The study was carried out in the Department of Radiodiagnosis and Imaging, Sree Balaji Medical College and Hospital, Chennai, a tertiary care teaching institution. Data collection was conducted over a period of nineteen months, from 2024 to 2025, during which eligible patients attending outpatient and inpatient services were recruited.

Study Population

The study population consisted of adult patients diagnosed with diabetes mellitus who had clinical features suggestive of diabetic peripheral neuropathy. Patients were referred for lower limb imaging evaluation from various departments, including General Medicine, Neurology, and Surgery. All participants underwent ultrasonographic evaluation of the tibial nerve as part of the study protocol.

Inclusion Criteria

Patients with a clinical diagnosis of diabetic peripheral neuropathy who were undergoing lower limb arterial Doppler or ultrasound evaluation were included in the study. Patients presenting with diabetic foot complications were also included, provided they met the diagnostic criteria for diabetic neuropathy.

Exclusion Criteria

Patients with a prior history of surgical procedures involving trauma to or excision of the tibial nerve were excluded. Individuals with deep vein thrombosis, leprosy, neurofibromatosis, tuberous sclerosis, Sturge–Weber syndrome, Guillain–Barré syndrome, chronic inflammatory demyelinating polyneuropathy, or ganglion cysts affecting the tibial nerve were excluded to avoid confounding structural nerve changes unrelated to diabetes.

Sample Size Estimation

The sample size was calculated using the standard formula for estimation of mean, based on previously reported variability in tibial nerve cross-sectional area [21]. The calculation was performed using a Z value of 1.96 corresponding to a 95% confidence interval, a standard deviation of 13.39, and an allowable error of 3. Based on this calculation, the minimum required sample size was determined to be 76.5, which was rounded up to a final sample size of 77 participants.

Sampling Method

Eligible patients who met the inclusion and exclusion criteria during the study period were recruited using a consecutive sampling method until the required sample size was achieved.

Ultrasonography Equipment and Technique

High-resolution ultrasonography was performed using a linear array transducer with a high frequency suitable for peripheral nerve imaging. All examinations were conducted by a radiologist experienced in musculoskeletal and neuromuscular ultrasound. Patients were positioned comfortably in the supine or prone position as appropriate, with the ankle slightly externally rotated to allow optimal visualization of the tibial nerve.

The tibial nerve was identified posterior to the medial malleolus and traced proximally to ensure accurate identification. Transverse images were obtained at standardized anatomical levels, and the nerve was visualized as an oval or round structure with a characteristic honeycomb appearance. The cross-sectional area of the tibial nerve was measured by tracing along the inner border of the hyperechoic epineurium using the continuous trace method. Care was taken to avoid excessive probe pressure to prevent artificial compression of the nerve.

Clinical Assessment of Neuropathy

All patients had a prior clinical diagnosis of diabetic peripheral neuropathy established by the referring physician based on history, physical examination, and relevant clinical investigations. Clinical details

including duration of diabetes, presence of neuropathic symptoms such as numbness, tingling, burning sensation, and pain, as well as the presence of diabetic foot complications, were recorded from medical records and patient interviews.

Data Collection

Demographic details and relevant clinical history were obtained through patient interviews and review of medical records. Ultrasonographic measurements of the tibial nerve were recorded at the time of examination and documented in the study records. Tibial nerve cross-sectional area values were noted for each participant for subsequent statistical analysis. All ultrasonographic measurements were performed using a standardized imaging protocol to ensure consistency and to minimize observer-related variability.

Statistical Analysis

Collected data were entered into a spreadsheet and analyzed using appropriate statistical software. Descriptive statistics were used to summarize demographic variables and tibial nerve cross-sectional area measurements. The association between tibial nerve cross-sectional area and clinical neuropathy characteristics was assessed using suitable inferential statistical tests. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee of Sree Balaji Medical College and Hospital prior to initiation of the study. Written informed consent was obtained from all participants in both English and the local language. Patient confidentiality was strictly maintained, and all data were used exclusively for academic and research purposes. The study involved no invasive procedures, and no additional risk was posed to participants beyond routine ultrasonographic examination.

Results:

Table 1. Baseline demographic and clinical characteristics of the study participants (N = 77)

Variable	Category	n (%) / Mean ± SD
Age group (years)	30–39	14 (18.2)
	40–49	21 (27.3)
	50–59	26 (33.8)
	≥60	16 (20.7)
Sex	Male	46 (59.7)
	Female	31 (40.3)
Duration of diabetes (years)	Mean ± SD	9.6 ± 4.1
HbA1c (%)	Mean ± SD	8.4 ± 1.3
Poor glycaemic control (HbA1c ≥8%)	Yes	49 (63.6)
	No	28 (36.4)
Diabetic foot	Present	28 (36.4)
	Absent	49 (63.6)
NCS-confirmed diabetic neuropathy	Present	77 (100.0)

Table 1 summarizes the baseline demographic and clinical characteristics of the study participants. The majority belonged to the 50–59 years age group (26, 33.8%), followed by the 40–49 years group (21, 27.3%). Males constituted 46 (59.7%) participants, while females accounted for 31 (40.3%). The mean duration of diabetes was 9.6 ± 4.1 years, and the mean HbA1c was 8.4 ± 1.3%, with 49 (63.6%) patients having poor glycaemic control (HbA1c ≥8%). Diabetic foot was present in 28 (36.4%) patients. All participants (77, 100%) had diabetic neuropathy confirmed by nerve conduction studies.

Table 2. Tibial nerve cross-sectional area and neuropathy severity (N = 77)

Variable	Category	n (%) / Mean ± SD
Neuropathy severity (TCNS)	Mild	24 (31.2)
	Moderate	32 (41.6)
	Severe	21 (27.3)
Right tibial nerve CSA (mm²)	Mean ± SD	13.8 ± 2.4
Left tibial nerve CSA (mm²)	Mean ± SD	13.6 ± 2.3
CSA category	Normal (≤10 mm²)	11 (14.3)
	Mild increase (10.1–12 mm²)	18 (23.4)
	Significant increase (>12 mm²)	48 (62.3)

Table 2 shows the severity of diabetic neuropathy and tibial nerve cross-sectional area (CSA). Moderate neuropathy was the most frequent category (32, 41.6%), followed by mild (24, 31.2%) and severe neuropathy (21, 27.3%). The mean CSA measured 13.8 ± 2.4 mm² on the right and 13.6 ± 2.3 mm² on the left. A majority of patients (48, 62.3%) demonstrated significantly enlarged tibial nerve CSA (>12 mm²), whereas only 11 (14.3%) had CSA within the normal range.

Table 3. Comparison of tibial nerve CSA according to neuropathy severity

Neuropathy severity	Mean CSA (mm²) ± SD	F value	p-value
Mild	11.6 ± 1.3	**28.7**	**<0.001***
Moderate	13.9 ± 1.6		
Severe	16.2 ± 1.9		

*One-way ANOVA.

Table 3 demonstrates a progressive increase in tibial nerve CSA with increasing neuropathy severity. Patients with mild neuropathy had a mean CSA of 11.6 ± 1.3 mm², which increased to 13.9 ± 1.6 mm² in moderate neuropathy and 16.2 ± 1.9 mm² in

severe neuropathy. One-way ANOVA showed that these differences were highly significant ($F = 28.7$, $p < 0.001$), indicating that tibial nerve enlargement increases significantly with worsening diabetic neuropathy.

Figure 1: Association Between CSA Categories and Neuropathy Severity

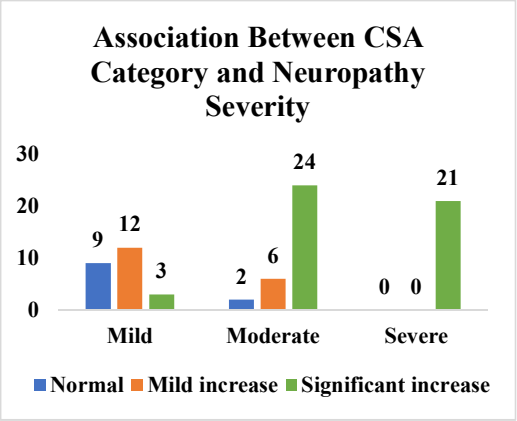

Figure 1 shows the distribution between tibial nerve cross-sectional area (CSA) categories and the severity of diabetic neuropathy. Patients with normal CSA values were predominantly found in the mild neuropathy group, with 9 cases, and only 2 cases in the moderate group, while none were observed in the severe neuropathy group. Similarly, patients with mildly increased CSA were limited to the mild and moderate neuropathy groups and were absent in the severe category.

In contrast, significantly increased CSA was predominantly observed in patients with moderate and severe neuropathy, with 24 cases in the moderate group and 21 cases in the severe group, while only 3 cases were seen in the mild neuropathy group. This distribution demonstrates a clear shift toward higher CSA categories with increasing neuropathy severity, indicating a strong association between tibial nerve enlargement and neuropathy severity. These findings support the role of tibial nerve CSA as a useful structural marker for grading the severity of diabetic neuropathy.

Table 4. Correlation of tibial nerve CSA with clinical variables

Variable	Correlation coefficient (r)	p value
TCNS score	+0.71	<0.001*
Duration of diabetes	+0.64	<0.001*
HbA1c	Positive association	<0.001*
Right vs Left CSA	Mean difference = 0.2 mm²	0.42

Table 4 demonstrates significant positive correlations between tibial nerve CSA and important clinical variables. CSA showed a strong positive correlation with TCNS score ($r = 0.71$, $p < 0.001$) and duration of diabetes ($r = 0.64$, $p < 0.001$), indicating that increasing neuropathy severity and longer duration of diabetes are associated with greater nerve enlargement. Patients with poorer glycaemic control also demonstrated significantly higher CSA ($p < 0.001$). There was no significant difference between right and left tibial nerve CSA ($p = 0.42$), confirming the bilateral symmetrical nature of diabetic peripheral neuropathy.

Table 5. Multivariate predictors of tibial nerve cross-sectional area

Predictor	β coefficient	p value
TCNS score	0.48	<0.001*
Duration of diabetes	0.31	0.002*
HbA1c	0.27	0.004*
Age	0.09	0.28

Table 5 presents the multivariate linear regression analysis identifying independent predictors of tibial nerve CSA. Neuropathy severity assessed by TCNS was the strongest independent predictor ($\beta = 0.48$, $p < 0.001$), followed by duration of diabetes ($\beta = 0.31$, $p = 0.002$) and HbA1c ($\beta = 0.27$, $p = 0.004$). Age was not independently associated with CSA ($p = 0.28$). These findings indicate that nerve enlargement is primarily influenced by neuropathy severity and metabolic control rather than chronological age.

Table 6. Diagnostic performance of tibial nerve CSA (>12 mm²) for diabetic neuropathy

Parameter	Value (%)
Sensitivity	82.4
Specificity	76.1
Positive predictive value (PPV)	85.0
Negative predictive value (NPV)	71.4
Overall diagnostic accuracy	79.2

Table 6 summarizes the diagnostic performance of a tibial nerve CSA cut-off value of >12 mm² for identifying clinically significant diabetic neuropathy. The cut-off demonstrated a sensitivity of 82.4% and specificity of 76.1%, with a PPV of 85.0% and an NPV of 71.4%. The calculated overall diagnostic accuracy was 79.2%, indicating that high-resolution ultrasonography of the tibial nerve provides good diagnostic performance and may serve as a useful, non-invasive adjunct for evaluating diabetic peripheral neuropathy.

Discussion

The present study demonstrates that high-resolution ultrasonography can reliably detect structural enlargement of the tibial nerve in patients with diabetic peripheral neuropathy. In this cohort of 77 patients with type 2 diabetes mellitus and electrophysiologically confirmed neuropathy, tibial nerve cross-sectional area measured at the medial malleolus was bilaterally symmetrical and showed a progressive increase with worsening neuropathy severity, longer duration of diabetes, and poorer

glycaemic control. A strong positive correlation was observed between tibial nerve CSA and Toronto Clinical Neuropathy Score, and multivariate analysis identified neuropathy severity, duration of diabetes, and HbA1c as independent predictors of CSA enlargement. These findings indicate that tibial nerve CSA reflects both structural nerve involvement and clinical disease burden in diabetic neuropathy.

Wang and colleagues conducted a retrospective study in China involving patients with type 2 diabetes and diabetic peripheral neuropathy, assessing ultrasound characteristics of the tibial nerve [61]. They reported significantly increased tibial nerve CSA in neuropathic patients compared to non-neuropathic diabetic controls, with mean CSA values commonly exceeding 12 mm² in moderate to severe neuropathy. These findings closely parallel the present study, where the majority of patients demonstrated significantly increased CSA. The similarity may be attributed to comparable study populations consisting of long-standing type 2 diabetes patients and the use of standardized medial malleolar measurement sites. Minor differences in absolute CSA values may reflect variations in disease duration and glycaemic control between cohorts. Hana and colleagues evaluated lower limb peripheral nerve involvement in Egyptian type 2 diabetes patients using neuromuscular ultrasound [22]. Their cross-sectional study revealed that tibial nerve CSA was significantly larger in patients with clinically and electrophysiologically confirmed neuropathy, and CSA values increased progressively with neuropathy severity. This trend is strongly supported by the present findings, where mean CSA increased from mild to severe neuropathy with a highly significant result. The concordance between studies suggests that tibial nerve enlargement is a reproducible marker of disease severity across different populations.

Lai and colleagues employed high-resolution ultrasound combined with shear wave elastography in a large Chinese cohort to stratify diabetic neuropathy severity [23]. They demonstrated that CSA enlargement and increased nerve stiffness both correlated strongly with clinical neuropathy grades. While elastography was not performed in the present study, the strong positive correlation between CSA and Toronto Clinical Neuropathy Score mirrors their structural–clinical association. The absence of elastography in the current study may explain slightly lower diagnostic sensitivity compared to their multimodal approach, yet the CSA-alone performance remained robust. Elshimy and colleagues investigated elastography and high-resolution ultrasound as early predictors of diabetic peripheral neuropathy in an Egyptian population [24]. They reported that tibial nerve CSA enlargement could be detected even in patients with early or subclinical neuropathy, preceding marked electrophysiological abnormalities. In contrast, all patients in the present study had abnormal nerve conduction studies by design, which explains the higher mean CSA values observed. This difference underscores the influence of disease stage on measured nerve size and supports the concept that CSA enlargement progresses with neuropathy severity.

Singh and colleagues established reference values for tibial nerve CSA in healthy Indian adults by high-resolution ultrasound [25]. They reported normal CSA values generally ≤10 mm² at the medial malleolus. When compared with these Indian normative data, the present study demonstrates a clear pathological shift, with only a minority of patients falling within the normal range and the majority exhibiting significant enlargement. This direct comparison strengthens the validity of CSA thresholds used in the current analysis. Dhanapalaratnam and colleagues evaluated the diagnostic accuracy of nerve ultrasonography for detecting diabetic peripheral neuropathy in type 2 diabetes [26]. They reported good sensitivity and specificity for CSA-based diagnosis, comparable to electrophysiological testing. In the present study, a tibial nerve CSA cut-off of >12 mm² demonstrated a sensitivity of 82.4% and specificity of 76.1% for identifying clinically significant neuropathy. The similarity in diagnostic performance reinforces the utility of tibial nerve CSA as a non-invasive diagnostic marker, particularly in settings where nerve conduction studies may not be readily available.

Multiparametric high-resolution ultrasound assessment has increasingly demonstrated the structural involvement of the tibial nerve in diabetic peripheral neuropathy. In an Egyptian cross-sectional study conducted by Elsayed and colleagues, evaluation of tibial nerve cross-sectional area, echogenicity, and elastographic stiffness showed significantly higher CSA values in neuropathic patients compared with controls, with a progressive increase across advancing neuropathy grades [27]. These observations are closely comparable to findings of the present study, in which mean tibial nerve CSA increased progressively from mild to severe neuropathy. The concordance of results across geographically distinct populations supports tibial nerve enlargement as a robust structural marker of diabetic neuropathy, relatively independent of ethnic variation.

The clinical applicability of tibial nerve ultrasound has been further emphasized in focused reviews. Al-Mendalawi and colleagues highlighted that posterior tibial nerve CSA enlargement represents a consistent sonographic feature in adults with type 2 diabetes mellitus and diabetic peripheral neuropathy, underlining the technique's accessibility

and reproducibility in routine practice [28]. The present study reinforces this observation by demonstrating bilateral and symmetrical tibial nerve enlargement with no significant side-to-side difference, a pattern characteristic of metabolic neuropathies rather than focal compressive nerve disorders.

The diagnostic utility of tibial nerve ultrasonography has also been evaluated in comparative clinical studies. In a cross-sectional analysis, Riazi and colleagues demonstrated that tibial nerve CSA was significantly larger in neuropathic patients than in non-neuropathic diabetics, with reasonable sensitivity and specificity for CSA-based diagnosis [29]. In the present study, a CSA cut-off value of >12 mm² yielded sensitivity and specificity values comparable to those reported by Riazi and colleagues. The slight differences in diagnostic performance may be due to variations in study design, particularly the inclusion of exclusively nerve-conduction-confirmed neuropathy cases in the present cohort.

Evidence from Indian populations provides important contextual validation. Singh and colleagues evaluated peripheral nerves using high-resolution ultrasound in Indian patients with diabetic peripheral neuropathy and reported tibial nerve CSA values commonly exceeding 12 mm² in neuropathic patients, compared with normal reference values ≤10 mm² [30]. When compared with these Indian data, the present study demonstrates a clear pathological shift, with the majority of patients showing CSA values above the normal range, reinforcing the diagnostic applicability of tibial nerve ultrasound in the Indian setting.

Strengths and Limitations

The present study possesses several strengths that enhance its methodological rigor and clinical relevance. A major strength is the application of high-resolution ultrasonography, a non-invasive, widely available, and cost-effective modality that allows real-time visualization of peripheral nerves without exposing patients to radiation or contrast agents. The use of standardized anatomical landmarks and uniform measurement techniques minimized variability and improved reproducibility. The inclusion of patients with clinically and electrophysiologically confirmed diabetic peripheral neuropathy ensured diagnostic accuracy, while the exclusion of patients with alternative causes of peripheral nerve pathology enhanced the specificity of the findings.

Despite these strengths, several limitations must be acknowledged. The hospital-based design may limit generalizability to the wider diabetic population, as patients presenting to tertiary care centers are more likely to have advanced disease. The cross-sectional nature of the study restricts the ability to establish temporal relationships or causal inferences. Longitudinal follow-up studies would be necessary to determine whether changes in tibial nerve morphology precede clinical neuropathy or predict disease progression. The absence of elastographic assessment and advanced quantitative ultrasound parameters limited the ability to evaluate nerve stiffness and internal architecture. Inter-observer variability analysis was not included, as all examinations were performed by a single observer. Additionally, nerve conduction parameters were used for confirmation of neuropathy but were not quantitatively correlated with ultrasonographic measurements, which could have strengthened structure–function analysis. Finally, glycaemic variability, medication history, and comorbid conditions such as dyslipidaemia or hypertension were not analyzed in detail.

Clinical Implications and Future Directions

The findings of this study have several important clinical implications. Tibial nerve ultrasonography provides objective, non-invasive, and reproducible evidence of structural nerve involvement in diabetic peripheral neuropathy. The strong correlation between CSA and clinical neuropathy severity suggests that ultrasound may serve as a useful adjunct to clinical and electrophysiological assessment. The identification of a practical diagnostic cut-off with good sensitivity and specificity supports the potential role of ultrasound in screening and early detection of neuropathy, particularly in resource-limited settings where advanced neurophysiological testing may not be readily available. The bilateral, symmetrical pattern of nerve enlargement observed reinforces the diagnosis of metabolic neuropathy rather than focal compressive pathology.

Future research should focus on longitudinal studies to evaluate the progression of structural nerve changes over time and their response to therapeutic interventions. Multicentric studies with larger sample sizes and standardized protocols would enhance generalizability. Incorporation of advanced ultrasound parameters such as elastography and echogenicity analysis may provide additional insight into nerve tissue composition and stiffness. Correlation with small-fibre neuropathy assessment and quantitative electrophysiological parameters would strengthen structure–function analysis. Finally, studies evaluating the cost-effectiveness of incorporating peripheral nerve ultrasound into routine diabetic care would inform healthcare policy and clinical practice guidelines.

Conclusion

In conclusion, the present study demonstrates that high-resolution ultrasonography is a valuable modality for assessing structural changes of the tibial nerve in patients with diabetic peripheral neuropathy. Measurement of tibial nerve cross-sectional area provides objective morphological evidence of nerve involvement and reflects the burden of neuropathic disease. The findings support

the concept that diabetic peripheral neuropathy is not solely a functional disorder but is accompanied by measurable structural alterations in peripheral nerves. By establishing a clear association between tibial nerve enlargement and clinical neuropathy severity, the study highlights the potential role of ultrasound as an adjunct to clinical and electrophysiological evaluation. The non-invasive nature, accessibility, and reproducibility of ultrasound make it particularly suitable for routine clinical use, especially in resource-limited settings. Incorporation of peripheral nerve ultrasound into the diagnostic algorithm may enhance comprehensive assessment of diabetic neuropathy and facilitate timely intervention. Further longitudinal and multicentric studies integrating ultrasound with functional, metabolic, and clinical parameters are warranted to establish its role in screening, prognostication, and monitoring therapeutic response.

References:

1. Feldman EL, Callaghan BC, Pop-Busui R, et al. *Diabetic Neuropathy*. 2nd ed. New York: Springer; 2019.
2. Boulton AJM, Vinik AI, Arezzo JC, et al. *Diabetic Neuropathies: A Statement by the American Diabetes Association*. Alexandria: ADA Press; 2005.
3. Peer S, Bodner G. *High-Resolution Sonography of the Peripheral Nervous System*. 2nd ed. Berlin: Springer-Verlag; 2013.
4. Jacobson JA. *Fundamentals of Musculoskeletal Ultrasound*. 3rd ed. Philadelphia: Elsevier; 2018.
5. Hobson-Webb LD, Cartwright MS. *Neuromuscular Ultrasound*. Oxford: Oxford University Press; 2016.
6. Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, Sosenko JM, Ziegler D. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care. 2017 Jan;40(1):136-154. doi: 10.2337/dc16-2042. PMID: 27999003; PMCID: PMC6977405.
7. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R; IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019 Nov;157:107843. doi: 10.1016/j.diabres.2019.107843. Epub 2019 Sep 10. PMID: 31518657.
8. Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P, Lauria G, Malik RA, Spallone V, Vinik A, Bernardi L, Valensi P; Toronto Diabetic Neuropathy Expert Group. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care. 2010 Oct;33(10):2285-93. doi: 10.2337/dc10-1303. Erratum in: Diabetes Care. 2010 Dec;33(12):2725. PMID: 20876709; PMCID: PMC2945176.
9. Boulton AJ. The pathway to foot ulceration in diabetes. Med Clin North Am. 2013 Sep;97(5):775-90. doi: 10.1016/j.mcna.2013.03.007. Epub 2013 Apr 29. PMID: 23992891.
10. Malik RA, Tesfaye S, Ziegler D. Medical strategies to reduce amputation in patients with type 2 diabetes. Diabet Med. 2013 Aug;30(8):893-900. doi: 10.1111/dme.12169. PMID: 23445087.
11. Vinik AI, Nevoret ML, Casellini C, Parson H. Diabetic neuropathy. Endocrinol Metab Clin North Am. 2013 Dec;42(4):747-87. doi: 10.1016/j.ecl.2013.06.001. PMID: 24286949.
12. Feldman EL, Nave KA, Jensen TS, Bennett DLH. New Horizons in Diabetic Neuropathy: Mechanisms, Bioenergetics, and Pain. Neuron. 2017 Mar 22;93(6):1296-1313. doi: 10.1016/j.neuron.2017.02.005. PMID: 28334605; PMCID: PMC5400015.
13. Callaghan BC, Cheng HT, Stables CL, Smith AL, Feldman EL. Diabetic neuropathy: clinical manifestations and current treatments. Lancet Neurol. 2012 Jun;11(6):521-34. doi: 10.1016/S1474-4422(12)70065-0. Epub 2012 May 16. PMID: 22608666; PMCID: PMC4254767.
14. Dyck PJ, Albers JW, Andersen H, Arezzo JC, Biessels GJ, Bril V, Feldman EL, Litchy WJ, O'Brien PC, Russell JW; Toronto Expert Panel on Diabetic Neuropathy. Diabetic polyneuropathies: update on research definition, diagnostic criteria and estimation of severity. Diabetes Metab Res Rev. 2011 Oct;27(7):620-8. doi: 10.1002/dmrr.1226. PMID: 21695763.
15. Ziegler D, Papanas N, Vinik AI, Shaw JE. Epidemiology of polyneuropathy in diabetes and prediabetes. Handb Clin Neurol. 2014;126:3-22. doi: 10.1016/B978-0-444-53480-4.00001-1. PMID: 25410210.
16. International Diabetes Federation. *IDF Diabetes Atlas*. 10th ed. Brussels: IDF; 2021.

17. Mohan V, Pradeepa R. Epidemiology of diabetes in different regions of India. *Health Adm*. 2009;22(1):1-18.
18. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, Adhikari P, Rao PV, Saboo B, Kumar A, Bhansali A, John M, Luaia R, Reang T, Ningombam S, Jampa L, Budnah RO, Elangovan N, Subashini R, Venkatesan U, Unnikrishnan R, Das AK, Madhu SV, Ali MK, Pandey A, Dhaliwal RS, Kaur T, Swaminathan S, Mohan V; ICMR–INDIAB Collaborative Study Group. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol. 2017 Aug;5(8):585-596. doi: 10.1016/S2213-8587(17)30174-2. Epub 2017 Jun 7. Erratum in: Lancet Diabetes Endocrinol. 2017 Aug;5(8):e5. doi: 10.1016/S2213-8587(17)30199-7. PMID: 28601585.
19. Shobhana R, Rao PR, Lavanya A, Vijay V, Ramachandran A. Foot care economics--cost burden to diabetic patients with foot complications: a study from southern India. J Assoc Physicians India. 2001 May;49:530-3. PMID: 11361267.
20. Tesfaye S. Advances in the management of diabetic peripheral neuropathy. Curr Opin Support Palliat Care. 2009 Jun;3(2):136-43. doi: 10.1097/SPC.0b013e32832b7df5. PMID: 19421063.
21. Sharath S, Kadavigere R, Maiya GA. Ultrasound Evaluations of Ankle and Foot Muscles in Diabetic Peripheral Neuropathy Systematic Review with Meta-Analysis. Curr Diabetes Rev. 2025;21(10):50-58. doi: 10.2174/0115733998310010240711051523. PMID: 39328136.
22. Hana MFF, Shaker ME, Ezzat WE, et al. Assessment of peripheral nerve affection of the lower limbs in type 2 diabetes using neuromuscular ultrasound. *Egypt J Neurol Psychiatry Neurosurg*. 2024;60(1):…
23. Lai ZH, She BY, Song ML, Wang JY, Zheng HQ, Wu KB, Jiang WT, Lyu GR. Role of nerve ultrasound and shear wave elastography in stratified diagnosis of diabetic peripheral neuropathy. Medicine (Baltimore). 2025 Nov 7;104(45):e45492. doi: 10.1097/MD.0000000000045492. PMID: 41204495; PMCID: PMC12599786.
24. Elshimy A, Elshimy G, Abouelhoda AM, Awad AA, Farouk O. Significance of high-resolution ultrasound imaging and elastography as early predictors of diabetic peripheral neuropathy. Ultraschall Med. 2025 May 5. English. doi: 10.1055/a-2589-8675. Epub ahead of print. PMID: 40324437.
25. Singh KP, Kaur S, Arora V. Reference Values for the Cross Sectional Area of Normal Tibial Nerve on High-resolution Ultrasonography. J Ultrason. 2022 Sep 1;22(90):e144-e152. doi: 10.15557/jou.2022.0024. PMID: 36482929; PMCID: PMC9714288.
26. Dhanapalaratnam R, Issar T, Poynten AM, Milner KL, Kwai NCG, Krishnan AV. Diagnostic accuracy of nerve ultrasonography for the detection of peripheral neuropathy in type 2 diabetes. Eur J Neurol. 2022 Dec;29(12):3571-3579. doi: 10.1111/ene.15534. Epub 2022 Sep 14. PMID: 36039540; PMCID: PMC9826521.
27. Elsayed, Walaa & Settein, Magdy & Elkhalek, Ahmed & Albehairy, Ahmed & Tharwat, Nehal. (2024). Multi-parametric high resolution ultrasound assessment of tibial nerve in diabetic peripheral neuropathy. Egyptian Journal of Radiology and Nuclear Medicine. 55. 10.1186/s43055-024-01402-z.
28. Al-Mendalawi MD. Posterior Tibial Nerve Ultrasound Assessment of Peripheral Neuropathy in Adults with Type 2 Diabetes Mellitus. J Med Ultrasound. 2024 Jul 10;32(3):275. doi: 10.4103/jmu.jmu_34_24. Erratum in: J Med Ultrasound. 2024 Nov 30;32(4):372. doi: 10.4103/JMU.JMU_118_24. PMID: 39310878; PMCID: PMC11414946.
29. Riazi S, Bril V, Perkins BA, Abbas S, Chan VW, Ngo M, Lovblom LE, El-Beheiry H, Brull R. Can ultrasound of the tibial nerve detect diabetic peripheral neuropathy? A cross-sectional study. Diabetes Care. 2012 Dec;35(12):2575-9. doi: 10.2337/dc12-0739. Epub 2012 Oct 1. PMID: 23033242; PMCID: PMC3507587.
30. Singh Y, Dixit R, Singh S, Garg S, Chowdhury N. High resolution ultrasonography of peripheral nerves in diabetic peripheral neuropathy. Neurol India. 2019 Jan-Feb;67(Supplement):S71-S76. doi: 10.4103/0028-3886.250719. PMID: 30688237.