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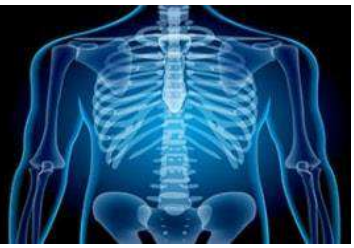

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Evaluation of Tibial nerve morphology by high resolution ultrasonography in diabetic patients with clinically suspected diabetic peripheral neuropathy: A cross sectional study

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Abstract
Background: Diabetic peripheral neuropathy is diagnosed by nerve conduction studies by presence of atypical parameters with respect to amplitude, latency as well as conduction velocity of nerve. In adjunct to current screening modalities, use of ultrasonography for evaluation of peripheral neuropathy in diabetic patients has been advocated as a promising diagnostic tool. The purpose of this study is to evaluate & measure Cross-sectional area of tibial nerve & maximum thickness of nerve fascicles of tibial nerve in diabetic patients with clinical suspicion of diabetic peripheral neuropathy by ultrasonography & its correlation with clinical symptoms, duration of diabetes & HbA1c.
Materials and methods: This cross-sectional study was conducted in Mahatma Gandhi Medical College and Research Institute from January 2021 to June 2022 amongst 30 clinically suspected diabetic peripheral neuropathy patients.
Results: The mean age, Hb1Ac & duration of diabetes was found to be 67.83, 10.08 & 21.27, with a male predominance (26 males & 4 females). Average Cross sectional area of tibial nerve, maximum thickness of nerve fascicles of tibial nerve & average total Toronto clinical neuropathy score was found to be 23.82 mm^2, 0.68 mm & 10.23 respectively. Correlation of duration of diabetes, HbA1c as well as Toronto neuropathy score against average Cross sectional area of tibial nerve, average maximum thickness of nerve fascicles of tibial nerve in both limbs was found to be statistically significant with a strong positive correlation.
Conclusion: High resolution ultrasonography is efficient in detecting morphological changes in tibial nerve in clinically suspected diabetic neuropathic patients. Cross-sectional area and maximum thickness of nerve fascicles of tibial nerve were found to be significantly higher than typical cut off values used in this study and high-resolution ultrasound is an important tool for diagnosis of diabetic peripheral neuropathy.

Keywords: Diabetes mellitus, Neuropathy, Tibial nerve morphology, ultrasonography

1. Introduction
On a global scale, there has been a constant upsurge in number of individuals suffering from diabetes. It is estimated that approximately 69.2 million people in India alone suffer from diabetes, with >50% of cases remaining undiagnosed [1]. Further, deleterious effects of diabetes mellitus have become a cause of concern [2].
Diabetes mellitus is a metabolic disorder characterized by defects in insulin secretion and or insulin action resulting in hyperglycemia. Type 1 Diabetes is a ketosis prone form of diabetes that results primarily from the autoimmune or idiopathic destruction of beta cells. Type 2 Diabetes results primarily from insulin resistance or concomitant beta cell secretory defect. Chronic hyperglycemia is associated with dysfunction and failure of various organs including development of nephropathy, retinopathy, neuropathy and vasculopathy [3].
Diabetic peripheral neuropathy is one of the major complications of diabetes mellitus, with prevalence rate of 30%, which increases with duration of diabetes. About 50% of patients will develop neuropathy during course of disease, primarily attributed to poor glycemic control [1].

The onset of diabetic peripheral neuropathy is instigated by chronic hyperglycemia which leads to osmotic swelling of peripheral nerves as well as advanced glycation end products, oxidative stress & altercations in lipids, which causes injury to axons, myelin sheath and alterations of neural structure [4].

Apart from tingling, numbness & pricking sensation; there may be absence of ankle reflexes & sensory disturbance in feet. Patients may also experience loss of vibration sense at toes, followed by pinprick, temperature & light touch sensations [1].

Tibial nerve is the largest terminal branch of sciatic nerve & lies superficial or posterior to popliteal vessels. It extends from superior angle to inferior angle of popliteal fossa, crossing popliteal vessels from lateral to medial side [1].

In diabetic peripheral neuropathy it is postulated that damage to tibial nerve is responsible for loss of motor function of superficial as well as deep muscles of calf & intrinsic muscles of sole; including sensory loss in sole of foot.[1] Therefore, use of ultrasonography as a fast real time imaging modality has advocated for detection & evaluation of diabetic neuropathy [4].

2. Materials and Methods

After obtaining approval from institutional review & ethical committee, this cross-sectional study was conducted in department of Radiodiagnosis, Mahatma Gandhi Medical College and Research Institute from January 2021 to June 2022 amongst 30 Diabetic patients with clinical suspicion of diabetic peripheral neuropathy who were referred by surgery and diabetology OPD meeting inclusion and exclusion criteria formed study population.

2.1 Inclusion criteria

Diabetic patients 18 years and above with clinical evidence of diabetic peripheral neuropathy.

2.2 Exclusion criteria

- Persons with non-diabetic causes of peripheral neuropathy.
- History of hereditary neuropathy, inflammatory neuropathy, nerve trauma, leprosy.

2.3 Procedure

After obtaining written and informed consent from diabetic patients with clinically suspected diabetic peripheral neuropathy. A brief history including age, sex, duration of diabetes, HbA1c values, clinical symptomatology (based on Toronto clinical neuropathy score) were recorded.

The severity of neuropathy is determined with Toronto clinical neuropathy score (TCNS) with its components as follows:

Symptom scores	Sensory test scores	Reflex scores
Foot pain	Pinprick	Knee reflexes
Numbness	Temperature	Ankle reflexes
Tingling	Light touch	
Weakness	Vibration	
Ataxia	Position sense	
Upper limb symptoms		
Symptoms are graded as	**Sensory test score graded as**	**Reflexes graded as**
0 = absent 1 = present	0 = normal 1 = abnormal	0 = normal 1 = reduced 2= absent

Total score ranges from 0 to maximum of 15. A score of 0 to 5 indicates absence of peripheral neuropathy, 6 to 8 indicates mild neuropathy, 9 to 11 indicates moderate neuropathy and more than 12 indicates severe peripheral neuropathy.

2.4 Ultrasound Technique

Ultrasonographic evaluation of the tibial nerve was performed with GENERAL ELECTRIC LOGIC S7 EXPERT. The ultrasonography was performed in a setting that affords adequate comfort and privacy to patient. The examination was done with patient lying in lateral position for an easy assessment of medial aspect of ankle and distal leg. Ultrasound linear transducer of 6-15 MHz was placed at 1, 3, 5 cm proximal to the medial malleolus of both lower limbs. The cross-sectional area (CSA) and maximum thickness of nerve fascicles (MTNF) of tibial nerve were measured in both lower limbs and average value of three measurements was taken into consideration. Cross-sectional area was calculated by largest antero-posterior dimension of the largest hypoechoic area in short axis view of tibial nerve. All sonographic images were obtained & interpreted by an experienced radiologist.

According to study conducted by kunwarpal singh *et al* Cross-sectional area & maximum thickness of nerve fascicles of tibial nerve for healthy non diabetic subjects was found to be ~ 12.4 +/- 1.01 mm^2 & 0.3mm respectively.[1] Considering these values as reference for healthy non diabetic individuals, the findings obtained in Cross-sectional area and maximum thickness of nerve fascicles of tibial nerve of clinically suspected diabetic peripheral neuropathy patients in this study was correlated & statistically analyzed.

2.5 Data collection

All data was entered into a Data Collection Proforma Sheet and was entered into Excel (MS Excel 2019). Other biographical details were also collected including age.

2.6 Statistical methods

Qualitative data was expressed as frequency and percentage. Quantitative data was expressed as mean and standard deviation. The association of cross-sectional area and maximum thickness of nerve fascicles of tibial nerve with rest of the variables like duration of diabetes, HbA1c values, Toronto clinical neuropathy score was expressed using Pearson correlation coefficient. Statistical analysis was carried out using SPSS version 22.0(IBM SPSS, US) software.

3. Results

The mean age of subjects was 67.83 ± 7.72, with a male predominance (87% males & 13% females) (Figure 4). Mean Hb1Ac was 10.08 ± 1.48 & the mean duration of diabetes was 21.27 ± 5.4 years. In this study we found average CSA, MTNF was found to be 23.82 ± 3.5 mm^2, 0.68 ± 0.2 mm respectively & mean total Toronto clinical neuropathy score was 10.23 ± 3.22. (Table 1).

Correlation of duration of diabetes against average Cross sectional area of tibial nerve & average maximum thickness of nerve fascicles of tibial nerve in both limbs was found to be statistically significant with a strong positive correlation (R Value: 0.967, 0.946; *P* value: <0.001). Correlation of HbA1c against average Cross sectional area of tibial nerve

& average maximum thickness of nerve fascicles of tibial nerve in both limbs was found to be statistically significant with a strong positive correlation (R Value: 0.943, 0.955 respectively; *P* value: <0.001). Correlation of Toronto clinical neuropathy score against average Cross sectional area of tibial nerve, average maximum thickness of nerve fascicles of tibial nerve in both limbs was found to be statistically significant with a strong positive correlation (R value: 0.95, 0.902 respectively; *P* value <0.001). (Table 2).

4. Discussion

Diabetes mellitus is a metabolic disorder that causes hyperglycemia as a result of defects in insulin secretion and/or action with type I caused by autoimmune or idiopathic destruction of beta cells, while type II is due to concurrent beta cell secretory defects or insulin resistance. Chronic hyperglycemia shows manifestations such as Nephropathy, retinopathy, neuropathy, & vasculopathy [5].

Chronic hyperglycemic patients show a prevalence rate of 30% for diabetic peripheral neuropathy, which is found to be higher in long-standing diabetics; that is increased with duration of the disease [6, 7].

Poor glycemic control is the main risk factor for the onset of diabetic polyneuropathy [8]. Abnormal parameters such as the amplitude, latency or the conduction velocity of the nerve are used to diagnose peripheral neuropathy by the neurologists & termed as diabetic peripheral neuropathy, more commonly in chronic diabetes patients [8, 9].

The search for better diagnostic modalities with a higher sensitivity & specificity rate is required to eliminate these shortcomings that are observed with the present nerve conduction studies, which are regarded as the gold standard. Further, their inability to detect peripheral neuropathy in mild forms may lead to the progression of the disease process [9]. These shortcomings can be overcome by the use of Ultra sonographic imaging [10].

We recorded a mean age of 67.83 ± 7.72 in this study, with definite male predominance. Similarly, Aaberg ML *et al*., [10] found 63 years old men experiencing neuropathic complications, about 4 years earlier than women (at 67 years).

The mean duration of the diabetes in this study was found to be 21.27 ± 5.4 years. In long-standing diabetic patients, usually after 10-20 years patients experience pain, tingling, or numbness in their hands as well as feet. Nisar MU *et al*., [11] found that the mean duration of diabetes to be 9 years (6.76), which can be attributed to the fact that we had greater number of elder patients in our study.

The mean HbA1c in our study was 10.08 ± 1.48. As per Stem MS *et al*. [12], patients with HbA1c score of 8.5 experience complications of DM, such as neuropathy, retinopathy, or nephropathy.

In current study, we also found a very strong positive correlation between HbA1c with Cross-sectional area and maximum thickness of nerve fascicles of tibial nerve (R Value: 0.943, 0.955 respectively; *P* value: <0.001). This finding is similar to the study conducted by Singh K et al. [1] in which Cross-sectional area of tibial nerve correlated significantly with HbA1c levels at $p<0.001$.

Abraham A *et al*. [13], observed worse polyneuropathy in lower limbs on all measures and worse electrophysiological parameters and vibration perception thresholds with higher TCNS severity grades & concluded that TCNS is a valid and reliable scale for a wide range of polyneuropathies, in terms of diagnosis and clinical staging. The mean total Toronto clinical neuropathy score in our study was 10.23 ± 3.22 (moderate severity).

Ultrasound allows visualization of peripheral nerves in upper & lower limbs, including cervical roots and brachial plexus. However, deeper nerves, like proximal sciatic nerve and lumbosacral plexus, are more challenging to visualize even with the use of ultrasound.

The observations of tibial nerve from ultrasonography in our study were as follows

- Tibial nerve appeared like a typical "honeycomb" on transverse scans, with ovoid hypoechoic fascicles scattered throughout a milieu of hyperechoic perineural connective tissue.
- Fascicles are visible longitudinally as bands of linear hypoechoic tissue.
- Epineurium appears hyperechoic, due to presence of dense connective tissue with high acoustic impedance.

The Average cross sectional area & Average maximum thickness of nerve fascicles of tibial nerve of both limbs in this study was 23.82 ± 3.5 mm^2 & 0.68 ± 0.2 mm respectively which were significantly higher than the reference values (12.4 +/- 1.01 mm^2 & 0.3mm respectively) taken from Singh K *et al* [1] for healthy non diabetic individuals used in this study.

According to the TCNS system, Chandrasekar HM *et al*., [14] found that with an increase in the grade of DPN severity, there was a demonstrable increase in the Cross-Sectional Area of Posterior Tibial Nerve and maximum thickness of nerve fascicles of tibial nerve. In our study, we also recorded a very strong positive correlation between Toronto neuropathy score with Cross-sectional area and maximum thickness of nerve fascicles of tibial nerve (R Value: 0.950, 0.902 respectively; *P* value: <0.001).

In a study conducted by Fateh *et al*., [15] demonstrated a significant correlation between the number of neuropathies, the mean diabetes duration, and the development of retinopathy. By performing a nerve conduction study, 121 (97%) diabetic patients were found to have neuropathy. Of these, 15 (12%) had mononeuropathy (which consisted of 33% sensory and 67% motor neuropathy) and 106 (85%) had polyneuropathy (which consisted of 31% motor and 69% sensorimotor neuropathy). In the current study, we also found a very strong positive correlation between duration of diabetes with average Cross-sectional area of tibial nerve and maximum thickness of nerve fascicles of tibial nerve in both limbs in mm^2 & mm (R Value: 0.967, 0.946; *P* value: <0.001).

Limitations in our study: though USG is a good modality due to its high resolution, because of operator variation the results could vary between different persons/equipment and sample size in this study is small which may influence statistical significance.

Figures

A Case of 80-year old male diabetic patient with severe peripheral neuropathy (TCNS–14, HbA1c–12.5, duration of diabetes–31 years)

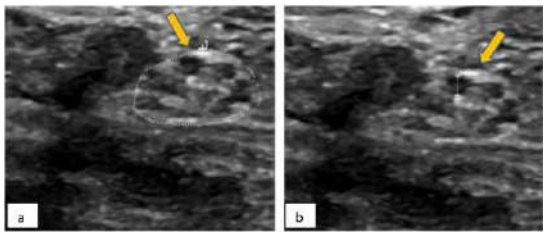

Fig 1: USG image shows a swollen Tibial nerve with a) CSA 28.5 mm^2 and b) MTNF of 1.1 mm measured at 1 cm proximal to upper end of medial malleolus

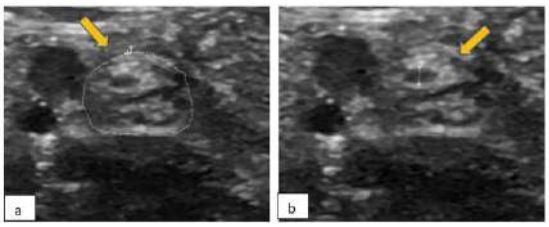

Fig 2: USG image shows a swollen Tibial nerve with a) CSA 29 mm^2 and b) MTNF of 1.1mm measured at 3 cm proximal to upper end of medial malleolus

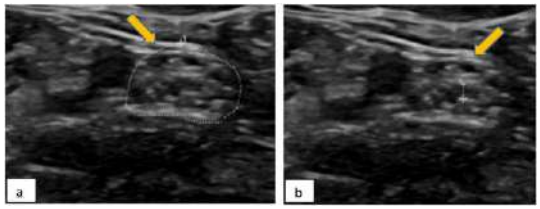

Fig 3: USG image shows a swollen Tibial nerve with a) CSA 29 mm^2 and b) MTNF of 1.1 mm measured at 5 cm proximal to upper end of medial malleolus

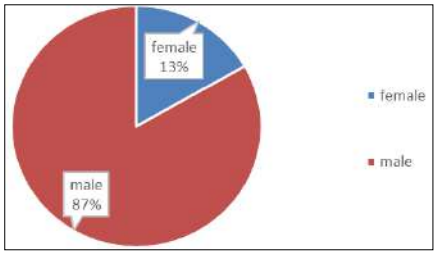

Fig 4: Pie chart of Sex in the study population (N=30)

Table 1: Clinical and Ultrasonography characteristics of study population (N=30)

Variables	Study population N = 30
Age in years (mean +/- SD)	67.83 +/- 7.72
Range	(54 - 84)
Male: Female	26: 4
Duration of diabetes in years (mean +/- SD)	21.27 +/- 5.4
Range	(12 - 34)
HbA1c levels in % (mean +/- SD)	10.08 +/- 1.48
Range	(7.5 - 13.5)
CSA of tibial nerve in mm2 (mean +/- SD)	23.82 +/- 3.5
Range	(18.5 - 29.5)
MTNF of tibial nerve in mm (mean +/- SD)	0.68 +/- 0.2
Range	(0.4 - 1.2)
TCNS (mean +/- SD)	10.23 +/- 3.22
Range	(6 - 16)

CSA–Cross sectional area; DN–Diabetic neuropathy; HRUS–High Resolution Ultrasonography; MTNF–maximum thickness of nerve fascicles TCNS–Toronto Clinical Neuropathy Score; US-Ultrasonography

Table 2: Correlation of Ultrasound tibial nerve morphological parameters with duration of diabetes, HbA1c, Toronto clinical neuropathy score

Parameter	Pearson coefficient	P value
Duration of Diabetes against average Cross-sectional area of tibial nerve in (mm^2)	0.967	<0.001
Duration of Diabetes against average maximum thickness of nerve fascicles of tibial nerve in (mm)	0.946	<0.001
HbA1c against average Cross-sectional area of tibial nerve in (mm^2)	0.943	<0.001
HbA1c against average Maximum thickness of nerve fascicles of tibial nerve in (mm)	0.955	<0.001
Toronto Clinical Neuropathy score against average Cross-sectional area of tibial nerve in (mm^2)	0.950	<0.001
Toronto Clinical Neuropathy score against average Maximum thickness of nerve fascicles of tibial nerve in (mm)	0.902	<0.001

5. Conclusion

Tibial nerve was chosen as the target nerve because it is one of first nerves to experience diabetic neuropathy and high resolution ultrasonography is efficient in diagnosing peripheral neuropathy in terms of the cross-sectional area as well as the maximum thickness of the nerve fascicles of the tibial nerve, which were found to be significantly higher than the typical cut off. In light of this, it can be said that high-resolution ultrasound of the tibial nerve is an important tool for diagnosis of diabetic peripheral neuropathy.

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7. Author's Contribution

Not available

8. Conflict of Interest

Not available

9. Financial Support

Not available

10. References

1. Singh K, Gupta K, Kaur S. High resolution ultrasonography of the tibial nerve in diabetic peripheral neuropathy. Journal of Ultrasonography. 2017;17(71):246-252.
2. Kumar A, *et al*. Ultrasonographic Examination of Peripheral Nerves in Diabetic Peripheral Neuropathy. Journal of Evolution of Medical and Dental Sciences. 2020;9(14):1131-1135.
3. Perkins BA, Bril V. Diabetic neuropathy: A review

emphasizing diagnostic methods. Clinical neurophysiology. 2003;114(7):1167-75.
4. Riazi S, *et al*. Can ultrasound of the tibial nerve detect diabetic peripheral neuropathy? A cross-sectional study. Diabetes care. 2012;35(12):2575-9.
5. Cade WT. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. Physical therapy. 2008;88(11):1322-35.
6. Pop-Busui R *et al*. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes care. 2017;40(1):136-54.
7. Sinnreich M, Taylor BV, Dyck PJ. Diabetic neuropathies: Classification, clinical features, and pathophysiological basis. The neurologist. 2005;11(2):63-79.
8. Papanas N, Ziegler D. Risk factors and comorbidities in diabetic neuropathy: an update 2015. The review of diabetic studies: RDS. 2015;12(1-2):48.
9. Carroll AS, Simon NG. Current and future applications of ultrasound imaging in peripheral nerve disorders. World Journal of Radiology. 2020;12(6):101.
10. Aaberg ML, Burch DM, Hud ZR, Zacharias MP. Gender differences in the onset of diabetic neuropathy. Journal of Diabetes and its Complications. 2008;22(2):83-7.
11. Nisar MU, *et al*. Association of diabetic neuropathy with duration of type 2 diabetes and glycemic control. Cureus. 2015,7(8).
12. Stem MS, *et al*. Impact of diagnosing diabetic complications on future hemoglobin A1c levels. Journal of Diabetes and its Complications. 2016;30(2):323-8.
13. Abraham A, *et al*. Toronto Clinical Neuropathy Score is valid for a wide spectrum of polyneuropathies. European Journal of Neurology. 2018;25(3):484-90.
14. Chandrasekhar HM, *et al*. Comparison of cross sectional area of posterior tibial nerve in diabetic peripheral neuropathy patients with that of healthy controls using high resolution ultrasonography: A cross sectional comparative descriptive study from Bangalore. Journal of Evidence Based Medicine and Healthcare. 2021;8(20):1466-1472.
15. Fateh HR, Madani SP, Heshmat R, Larijani B. Correlation of Michigan neuropathy screening instrument, United Kingdom screening test and electrodiagnosis for early detection of diabetic peripheral neuropathy. Journal of Diabetes & Metabolic Disorders. 2015;15(1):1-5.

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