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# Ultrasonogrpahic examination of peripheral nerves in diabetic peripheral neuropathy

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#### Abstract

Aim: Ultrasonographic examination of peripheral nerves in diabetic peripheral neuropathy patients (DPN) and comparison of findings with healthy controls.

**Methods:** 50 patients clinically diagnosed with diabetic peripheral neuropathy and 50 healthy non-diabetic subjects taken as controls were analysed. The cross sectional area (CSA)of the median nerve, ulnar nerve, common peroneal nerve and posterior tibial nerve was measured at predetermined sites. The mean CSA was calculated and compared among both groups.

**Results:** There was a significant increase in CSA of median nerve  $(11.00\pm1.64 \text{ mm}^2, 10.26\pm1.67 \text{ mm}^2 \text{ and } 9.98\pm1.67 \text{ mm}^2 \text{ at } 5 \text{ cms proximal to wrist crease, at mid forearm and at elbow joint respectively vs } 7.34\pm1.23 \text{ mm}^2, 6.80\pm0.80 \text{ mm}^2 \text{ and } 11.00\pm1.64 \text{ mm}^2)$ , ulnar nerve  $(8.30\pm1.34 \text{ mm}^2 \text{ and } 9.20\pm1.17 \text{ mm}^2 \text{ at wrist joint and behind medial epicondyle respectively vs } 6.90\pm0.86 \text{ mm}^2 \text{ and } 7.38\pm0.96 \text{ mm}^2)$ , common peroneal nerve  $(9.16\pm1.76 \text{ mm}^2 \text{ vs } 7.02\pm1.18 \text{ mm}^2 \text{ at eck of fibula})$  and posterior tibial nerve  $(9.08\pm1.71 \text{ mm}^2 \text{ vs } 6.86\pm0.99 \text{ mm}^2 \text{ at 3cms proximal to medial malleolus})$  in DPN patients as compared with healthy controls. The difference was statistically significant at p value of 0.001.

**Conclusion:** This study of confirms that the CSA of the peripheral nerves is larger in patients with DPN compared with healthy controls and that ultrasonography is a promising point-of-care screening tool for DPN.

Keywords: Ultrasonography, Peripheral nerves, Diabetic peripheral neuropathy, CSA

#### Introduction

Diabetes mellitus represents a spectrum of metabolic disorders which has become a major health challenge worldwide.<sup>1</sup> Both type 1 and 2 diabetes have peripheral neuropathy as one of the most common complication but these neuropathies have also been noted in those with no diabetes but impaired glucose tolerance and in prediabetics. <sup>2</sup>Diabetic neuropathy can greatly lower quality of life in diabetics and also increase mortality and morbidity.<sup>3</sup>Age, duration of diabetes, dyslipidemia, glycated hemoglobin, complications, microvascular macrovascular complications, and alcoholic status are risk factors for the development of peripheral neuropathy.<sup>4-6</sup> Diabetic neuropathy (DN) refers to signs and symptoms of neuropathy in a patient with diabetes in whom other causes of neuropathy have been excluded. Diabetic neuropathy has been classified symmetrical and asymmetrical.Distal as symmetrical polyneuropathy (DSPN) is the commonest subtype accounting for 75% DN and involves peripheral nerves of hands and feet bilaterally and symmetrically. Peripheral nerves of limbs may also be involved individually and asymmetrically.<sup>2</sup>

The sonographic study of peripheral nerves was pioneered by Bruno Fornage in 1988 when Bruno Fornage when he described the sonographic features of the peripheral nerves and associated masses.<sup>7</sup>Almost all the nerves including digital nerves can be imaged by ultrasonography. A high-frequency linear array probe (3-12 MHz) is used. The examination is started from a known anatomic landmark near the nerve. Once the nerve is localized in the short axis it is traced cranially and caudally to see for its contour and architectural abnormality. Movement of limb helps to differentiate nerve from tendons, whereas Color Doppler helps to differentiate nerves from vessels. Lymph nodes are spherical and show a fatty hilum and can be easily differentiated from nerves by their shape and inability to trace them in longitudinal axis.<sup>8</sup>

#### **Aims and Objectives**

The objectives of this study are:

To evaluate peripheral nerve pathology in diabetics by ultrasonography

To correlate clinical symptomatology with ultrasound findings

#### **Materials and Methods**

The study was conducted after approval from the institutional thesis and ethical committee. The main source of data for the study is patients from Guru Nanak Dev Hospital attached to Government Medical College, Amritsar.

50 patients were randomly selected from the referred patients with the clinical suspicion of diabetic peripheral neuropathy. 50 healthy non diabetics with no clinical evidence of peripheral neuropathy were also selected. Imaging was done using high frequency 3-12

MHz linear probe on MINDRAY DC-8 ultrasound system in the Department of Radiodiagnosis of Guru Nanak Dev Hospital, Amritsar. Informed consent was taken after explaining the procedure to the patient in his/her vernacular language.

#### **Inclusion criteria**

#### For patients

Patients with clinically suspected diabetic peripheral neuropathy (DPN).

#### For healthy normal volunteers:

A healthy non diabetic adult person with no clinical evidence of peripheral neuropathy.

#### **Exclusion criteria**

1) Children <18 years due to inability to provide informed consent.

2) Pregnant women

3) Persons with history InofJ. ChemeditearlyIed. Sci. (2018). 4(12): 65-75 neuropathy, inflammatory neuropathy and nerve trauma

#### **Observations and Results**

#### Table 1 Age and sex distribution of healthy volunteers (n = 50)

Age in years	Number of healthy volunteers	Sex		
		Male	Female	
<30	1(0%)	1(2%)	0(0%)	
30-40	19(38%)	15(30%)	4 (8%)	
41-50	19 (38%)	15(30%)	4 (8%)	
51-60	8(16%)	3(6%)	5(10%)	
61-70	3 (6%)	3(6%)	0(0%)	
>70	0(0%)	0(0%)	0(0%)	
Total	50	37 (74%)	13 (26%)	

The mean age of healthy volunteers was 44.76±8.85 years.

#### Table 2 Age and sex distribution DPN patients (n = 50)

Age in years	Number of healthy volunteers	Sex		
		Male	Female	
<30	0(0%)	0	0	
30-40	4	1	3	
41-50	11	7	4	
51-60	21	13	8	
61-70	13	11	2	
>70	1	0	1	
Total	50	32	18	

The mean age of DPN patients was 55.28±9.32 years.

#### Table 3 Comparison of mean Csa of median nerve at various levels in patients and healthy volunteers

Level of examination		Healthy volunteers (n=50)	Patients (n=50)	p-value
At 5 cm proximal	CSA range (min-Max) in mm <sup>2</sup>	5-10	8-14	
to wrist crease	Mean $\pm$ SD	7.34±1.23	11.00±1.64	0.001
At mid forearm	CSA range (min-Max) in mm <sup>2</sup>	5-8	8-13	
At find forearm	Mean $\pm$ SD	6.80±0.80	10.26±1.67	0.001
At elbow joint	CSA range (min-Max) in mm <sup>2</sup>	6-9	7-13	
	Mean $\pm$ SD	7.34±0.71	9.98±1.67	0.001

The mean CSA of median nerve in DPN patients was significantly greater than healthy volunteers at all three levels of examination.

Level of examination		Healthy volunteers (n=50)	Patients (n=50)	p-value
At wrist joint	CSA range (min-Max) in mm <sup>2</sup>	4-9	6-10	
	Mean ± SD	6.90±0.86	8.30±1.34	0.001
Behind medial epicondyle	CSA range (min-Max) in mm <sup>2</sup>	5-9	6-11	
	Mean ± SD	7.38±0.96	9.20±1.17	0.001

#### Table 4 Comparison of mean CSA of ulnar nerve at various levels in patients and healthy volunteers

The mean CSA of ulnar nerve in DPN patients was significantly greater than healthy volunteers at both levels of examination.

#### Table 5 Comparison of mean CSA of common peroneal nerve at neck of fibula inpatients and healthy volunteers

Level of examination		Healthy volunteers (n=50)	Patients (n=50)	p-value
Neck of fibula	CSA range (min-Max) in mm <sup>2</sup>	5-11	6-13	
	Mean $\pm$ SD	7.02±1.18	9.16±1.76	0.001

The mean CSA of common peroneal nerve in DPN patients was significantly greater than healthy volunteers at both levels of examination.

### Table 6 Comparison of mean CSA of posterior tibial nerve 3 cms above medial malleolus in patients and healthy volunteers

Level of examination		Healthy volunteers (n=50)	Patients (n=50)	p-value
Medial malleolus	CSA range (min-Max) in mm <sup>2</sup>	5-10	6-13	
Meurar maneorus	Mean $\pm$ SD	6.86±0.99	9.08±1.71	0.001

The mean CSA of posterior tibial nerve in DPN patients was significantly greater than healthy volunteers at both levels of examination.

#### Discussion

Out of 50 healthy volunteers included in the study, 37 were males and 13 were females. The mean age was 44.76±8.85 years.Out of 50 DPN patients included in study 32 were males and 18 were females. The mean age was 55.28±9.32 years. The mean duration of diabetes mellitus in DPN patients was  $13.72\pm5.23$ years.Ultrasonography was able to demonstrate median, ulnar, common peroneal and posterior tibial and nerves in all the healthy volunteers and DPN Peripheral nerves had patients. а characteristic honeycomb appearance on axial scans with a network of multiple rounded hypoechoic fascicle groups surrounded by hyperechoic perineurium and epineurium. None of the nerves demonstrated any intraneural vascularity. Ultrasonography depicted increase in CSA of peripheral nerves at multiple levels in clinically diagnosed patients with diabetic peripheral neuropathy as compared to healthy volunteers which included median nerve at 5 cms proximal to wrist crease, at mid forearm and at elbow joint; ulnar nerve at wrist joint and behind medial epicondyle; common peroneal nerve at neck of fibula and posterior tibial nerve at 3 cms above medial malleolus.

#### **Median Nerve**

The cross section area (CSA) of median nerve was  $>9 \text{ mm}^2$  in 84% patients at 5 cms proximal to wrist crease, in 64% at mid forearm & in 58% patients at elbow joint. While in majority of the healthy volunteers i.e in 96% 5cm proximal to wrist crease, in 100% at mid forearm and in 100% at elbow joint the median nerve CSA was <9

mm<sup>2</sup>. The mean CSA of median nerve in DPN patients was  $11.00\pm1.64 \text{ mm}^2$ ,  $10.26\pm1.67 \text{ mm}^2$  and  $9.98\pm1.67 \text{ mm}^2$  at 5 cms proximal to wrist crease, mid forearm and at elbow joint respectively which was significantly greater as compared to healthy volunteers (i.e.  $7.34\pm1.23 \text{ mm}^2$ ,  $6.80\pm0.80 \text{ mm}^2$  and  $11.00\pm1.64 \text{ mm}^2$ ) at all three levels (p 0.001). Our findings are in concordance with the Watanabe T et al<sup>9</sup> and Pitarokili K et al<sup>10</sup> who found that there is significant increase in the cross-sectional area of the median nerve in patients with diabetic peripheral neuropathy as compared with the controls.

#### **Ulnar Nerve**

In majority of the patients with DPN, the ulnar nerve cross section area was  $>8 \text{ mm}^2$  seen in 52% of cases at wrist joint and in 76% of patients behind medial epicondyle. While in majority of the healthy volunteers, the ulnar nerve mean cross section area was  $< 8 \text{ mm}^2$  seen in 98% of cases at wrist joint and in 90% of patients behind medial epicondyle. The mean CSA of ulnar nerve in DPN patients was  $8.30\pm1.34$  mm<sup>2</sup> and  $9.20\pm1.17$  mm<sup>2</sup> at wrist joint and behind medial epicondyle respectively which was significantly as compared to healthy volunteers (i.e.  $6.90\pm0.86$  mm<sup>2</sup> and  $7.38 \pm 0.96 \text{ mm}^2$ ) at both levels (p 0.001). Our findings are in concordance with the Pitarokoili K et al who found that there is significant increase in the cross-sectional area of the ulnar nerve in patients with **DPN** as compared to controls i.e.  $6.30 \pm 1.92 \text{ mm}^2 \text{ vs. } 5.0 \pm 0.94 \text{ mm}^2$ at wrist joint and 8.34±2.46 mm<sup>2</sup> vs. 5.99±1.57  $\mathbf{mm}^2$  behind medial epicondyle.<sup>10</sup>

Figure 1 : Median nerve CSA in healthy volunteer and DPN patient at level of elbow joint



Figure 1a



Figure 1b

Figure 1a Median nerve in a healthy volunteer at the level of elbow joint with CSA of 5 mm<sup>2</sup> Figure 1b Median nerve in a patient with DPN at the same level with CSA of 12 mm<sup>2</sup>. On Color Doppler no color flow was seen in the nerve Figure 2 Ulnar nerve CSA in healthy volunteer and DPN patient at level of wrist joint



Figure 2a



Figure 2b

Figure 2a Ulnar nerve in a healthy volunteer at the level of wrist joint with CSA of 4 mm<sup>2</sup> Figure 2b Ulnar nerve in a patient with DPN at the same level with CSA of 9 mm<sup>2</sup>. On Color Doppler no color flow was seen in the nerve

#### **Common Peroneal Nerve**

In majority of the patients with DPN, the common peroneal nerve cross section area was >8 mm<sup>2</sup> seen in 70% of cases. While in majority of the healthy volunteers, the common peroneal nerve mean cross section area was < 8 mm<sup>2</sup> seen in 92% of cases. The mean CSA of common peroneal nerve in DPN patients was  $9.16\pm1.76 \text{ mm}^2$  which was significantly greater as compared to healthy volunteers who had mean CSA of  $7.02\pm1.18$ mm<sup>2</sup>(p 0.001). The study by Pitarokoili et al also showed similar results where the mean CSA (in mm<sup>2</sup>) of **fibular nerve at fibular head** was greater in patients as compared to **controls i.e.**  $12.22\pm4.97 \text{ vs. } 7.2\pm1.89.^{10}$ 

#### **Posterior Tibial Nerve**

In majority of the patients with DPN, the posterior tibial nerve cross section area was  $>9 \text{ mm}^2$  seen in 56% of cases. While in majority of the healthy volunteers, the posterior tibial nerve mean cross section area was  $< 9 \text{ mm}^2$  seen in 98% of cases. The mean CSA of posterior tibial nerve in patient with DPN was  $9.08\pm1.71$  mm<sup>2</sup>, which was significantly higher than healthy volunteers where the mean CSA was  $6.86\pm0.99$  mm<sup>2</sup> (p value 0.001). The study by Pitarokoili and colleagues also showed similar results where the mean CSA (in mm<sup>2</sup>) of **posterior tibial nerve**was greater in patients as compared to controls i.e. 9.26 ± 3.33vs  $6.9 \pm 0.86$ mm<sup>2</sup>.<sup>10</sup>Similar findings were reported by Riazi S et al<sup>11</sup> that the mean CSA of the posterior tibial nerve was larger in patients with DPN than in control subjects.

### Figure 3: Common peroneal nerve CSA in healthy volunteer and DPN patient at level of neck of fibula



Figure 3a



Figure 3b

Figure 3a Common peroneal nerve in a healthy volunteer at the level of neck of fibula with CSA of 7 mm<sup>2</sup> Figure 3b Common peroneal nerve in a patient with DPN at the same level with CSA of 13 mm<sup>2</sup>

## Figure 4: Posterior tibial nerve CSA in healthy volunteer and DPN patient at level of 3 cms above medial malleolus



Figure 4a



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Figure 4a Posterior tibial nerve in a healthy volunteer at the level of 3 cms above medial malleolus with CSA of  $6 \text{ mm}^2$ 

Figure 4b Posterior tibial nerve in a patient with DPN at the same level with CSA of 13 mm<sup>2</sup>

#### Conclusion

Diabetes mellitus has become a major health challenge worldwide. Rapid urbanization has led to an increased prevalence of diabetes mellitus in India. Diabetes mellitus is associated with various major complications i.e. retinopathy, nephropathy and neuropathy which lead to a significant increase in morbidity and mortality. Diabetic peripheral neuropathy results in thickening of nerves. The diagnosis of diabetic peripheral neuropathy in Indian set up is mainly clinical. Conventional investigations include nerve conduction study which is minimally invasive and time consuming. Newer investigations like MRI are expensive along with being time consuming.

Ultrasonography of peripheral nerves is a valuable adjunctive modality in the diagnosis of diabetic peripheral neuropathy. This technique can non-invasively complement other diagnostic investigations like MRI. Increase in CSA demonstrated by ultrasonography may provide important information about neuropathy to the treating clinician.

#### Conflict of interest: None declared

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