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Original Article

Ultrasound as a Diagnostic Modality for the Involvement of Peripheral Nerves in Leprosy

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Leprosy is a major infectious cause of serious deformities which affects skin, nerves, eyes and limbs. In this study we have attempted to incorporate ultrasonography as an objective tool for the detection of early nerve thickening compared to healthy controls. A case control study was performed with 35 patients with leprosy as cases and 30 healthy controls. Clinical evaluation of bilateral ulnar, median and common peroneal nerves respectively was performed by two observers and they reached a consensus whether the nerve was thickened or not. Ultrasonography of these nerves was conducted and dimensions like cross sectional area and circumference was noted and compared with those of healthy subjects. Receiver operator characteristics and area under curve method was used to determine cut off values for nerve thickness of each nerve. All six examined nerves showed significant thickening in leprosy patients compared to controls. Nerve involvement was more common among males at 72.4%. Around 62.8% patients belonged to the Borderline spectrum followed by lepromatous, pure neural and tuberculoid at 17.1%, 11.4% and 5.7% respectively. One patient had histoid type of lepromatous leprosy with nodular lesions. Patients with leprosy had significantly higher number of thickened nerves with p value <0.001. Asymmetric nerve thickness was noted in 54.6%. Among 210 nerve points examined 86 were found to be clinically thickened and 138 were found to be thickened ultrasonographically (p<0.001). The most common sonographic finding was focal thickening (83.3%) followed by hypoechoicity (63%). Using receiver operator characteristics, nerve cross sectional area above 0.08cm sq. was found to be a predictor of nerve thickness. Ultrasound is a noninvasive modality that acts as an effective and objective marker of nerve thickening in leprosy. Besides detection of nerve thickening in leprosy, it can be used to identify structural changes in the nerve such as focal thickening and inflammation.

Key words: Ultrasonography, Peripheral nerve, Nerve thickening

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Introduction

Leprosy is a major infectious cause of serious deformities which affects skin, nerves, eyes and limbs (Rodrigues and Lockwood 2011). Early nerve changes include axonal atrophy and inflammation around the focus of infection, this provides a vascular port for the entry of *M. leprae* from perineurium to the endoneurium (Scollard 2000) which then gets engulfed by Schwann cells within the fascicle (Mattos et al 2011). Edema accompanies the inflammation (Iida et al 2007) causing peripheral nerve injury and demyelination (Lockwood et al 2011).

Wilder Smith and Van Brakel (2008) stated that clinical examination of peripheral nerve involvement by palpation is subjective to a wide inter-observer variability. Clinical examination is challenging due to the deeper course traversed by peripheral nerves (Scollard et al 1999). Other tools to test the integrity of nerve function include voluntary muscle testing (VMT), testing for sensation by graded Semmes Weinstein (SW) mono filaments and sweat test for autonomic function respectively.

Electroneuromyography (ENMG) can be used but requires specialized equipment, skilled technicians and is expensive (Rao and Jain 2013). Though electrophysiology is considered a standard investigation to evaluate neuropathy (Martinoli et al 2000a), the precise location and affection of surrounding tissues cannot be assessed thus making way for imaging studies like ultrasound to diagnose nerve involvement in leprosy (Thain and Downey 2002).

Small fibre sensory damage has been assessed by computerized quantitative sensory tests (QST), the somatosensory pathways has been evaluated by contact heat evoked potentials (CHEPS). The unmyelinated fibers of cornea can be examined by corneal confocal microscopy (CCM). These methods are known to improve the accuracy of diagnosis and treatment of neuropathy (Nascimento et al 2013).

According to Joshi (2011) histopathology aids in classifying spectrum of leprosy, evaluation of disease inactivity post treatment and also in confirming a case of relapse. However, clinico-histological concordance is not always seen (Patnaik et al 2014). In a study to evaluate histological features in skin biopsies of borderline leprosy patients presenting clinically with type 1 reaction. It was found that histologic findings of type 1 reaction in was seen in only 67.5% (27/40) patients with clinical features of reaction. On the other hand, histopathological features of reaction were seen in 20% (10/50) of patients who had no clinical features of a reaction. Occasional non specificity of invasive tests such as skin biopsy for histopathology warrants the need for newer and more novel approaches to reach a diagnosis. It is difficult to distinguish relapse from reaction in treated paucibacillary patients and to differentiate them from other granulomatous diseases like sarcoidosis, tuberculosis or a foreign body granuloma using histopathology.

Skin smears have a specificity of 100% with low sensitivity but scanty bacilli could be missed. Fear of transmission of HIV and hepatitis virus infections by this method is a disadvantage (Georgiev and McDougall 1988).

Ultrasonography uses the piezoelectric effect which converts electric energy to sound waves. The ultrasound unit comprises of a transducer, transmitter, image visualization and image storage device. The B mode ultrasound is based on brightness of a grid of grey dots that helps decipher various anatomical structures (Rosen et al 2014).

Ultrasonography is a non-invasive modality which is useful for studying changes at nerve sites and is

more cost-effective than other imaging procedures, such as magnetic resonance imaging. Current technological developments leading to improved image quality, reduced size of device, portability makes it possible for USG to become a useful tool where leprosy is endemic (Jain et al 2009).

USG can be used to calculate the cross sectional areas of peripheral nerves (Frade et al 2013). It is useful to study structural changes in nerve sites that cannot be biopsied for histopathology especially in mixed nerves that run the risk of muscle palsy, and is more cost effective than magnetic resonance imaging. Moreover, the nerve can be examined for a longer length than with MRI where it is limited to defined segments (Martinoli et al 2000b).

Ultrasound measurements showing increased nerve size are a sensitive indicator of the presence of neuropathy in leprosy (Elias et al 2009). The nerves are often palpably enlarged in leprosy, particularly in areas where they are superficial and in tissues that are typically cooler than core body temperature, for example, the ulnar nerve at the elbow and the fibular nerve at the fibular head (Rodrigues and Lockwood 2011).

Sonography and electrophysiology were considered the new methods for identifying ulnar nerve neuropathy in 21 consecutive Brazilian patients with leprosy, with clinical symptoms as the reference standard (Lolge et al 2005). This report in turn emphasized the role of sonography in the investigation of ulnar neuropathy due to leprosy. Ultrasound performed at the elbow in this study helped distinguish ulnar palsy due to leprosy from those due to nerve entrapment.

A study using vasomotor blood flow in the distribution of the ulnar nerve by Wilder-Smith et al (2000) showed that color Doppler measurements of blood flow in the ulnar artery by ultrasonography was sensitive and specific in identifying small fiber autonomic dysfunction in 12 patients with leprosy and 20 healthy controls.

In addition to enlargement, nerves in leprosy patients exhibit varying degrees of structural abnormalities such as fusiform enlargement or loss of fascicles, edema and increased neural vascularity which can be elicited by the Doppler mode on the USG machine (Lolge et al 2005). The ultrasound image of nerves is visualized as hypoechoic tubular fascicles within a hyperechoic background of epineurium (Silvestri et al 2005). Nerves in cross section appear as round to oval depending on the width of their anatomic passageways such as joints and osseofibrous tunnels and the perineural structures at each juncture. The nerves appear more homogeneous and hypoechoic at areas of tight packing of nerve fascicles. Under normal circumstances, the perineural and intraneural vasculature is not visualized on Doppler imaging modalities due to low blood volume and slow flow velocities. In addition ultrasound may also demonstrate muscle abnormalities such as atrophy and fat replacement (Kermarrec et al 2011).

Studies reveal that there is no distinguishing feature to identify tuberculoid from lepromatous forms of leprosy on imaging. Higher frequency and severity of reversal reactions results in greater disruption of nerve architecture on ultrasonography (Martinoli et al 2000a, b). The enlarged nerve is visualized at cubital tunnel for the ulnar nerve, carpal tunnel for the median nerve, the area of the fibular head and neck for the peroneal nerve, and the tarsal tunnel for the tibial nerve (Elias et al 2009). Though the modality has been in use for leprosy for more than 10 years, the long learning curve required to gain skills to visualize the nerves and interpret accurately and poor availability of high end machines has limited its use in this regard (Lolge et al 2005).

The nerve thickness is measured using the cross sectional area (Yesildag et al 2004). The commonly used methods are applying the formula at the site of maximal cross sectional area using calipers and the multiplication product of the transverse diameter, anteroposterior diameter and π/4. Direct method includes a manual trace of the nerve and applying an automated formula to calculate cross sectional area (Duncan et al 1999).

The advantages of using ultrasound include the ability to test for multiple nerve sites and a longer section of the same nerve for localized thickening. The modality may help mark sites for nerve decompression and revamp the need for nerve release surgeries, percutaneous nerve biopsies, guidance for local perineural injections which in turn would prevent or delay nerve compression and its sequelae. The response to steroids and anti reaction agents are assessed clinically to this day and ultrasound provides an objective method for the same (Bernardin and Thomas 1997). Ultrasonography can contribute to early recognition and management of nerve involvement. In this context, leprosy could prove to be a model disease for studying how a low-cost portable imaging technology can alter the diagnosis, treatment, and management of nerve disease (Mayans et al 2012). In this study we have attempted to incorporate ultrasonography as an objective tool for the detection of nerve thickening when compared to the highly subjective clinical palpation. The nerve dimensions like cross sectional diameters, circumference and cross sectional area have been determined, morphological characteristics like inflammation and hypoechoicity of nerve have been noted, further we have used receiver operator characteristics to determine a cut off value for nerve thickness.

Materials and Methods

After obtaining permission from Father Muller institutional Ethical Committee, Mangalore, a case control study was performed with 35 patients with newly detected leprosy as cases and 30 healthy controls. All clinically diagnosed cases of leprosy attending the Dermatology out-patient department and admitted patients at Father Muller Medical College Hospital, Mangalore were included the study. Convenient sampling technique was used. Age and sex matched healthy individuals who did not have leprosy were taken as controls for the study. The study period was between October 2014 to September 2015. Sample size was calculated using the formula

$N=Z\alpha^2\ p(1-p)/e^2$

Zα: 1.96 at 95% confidence interval

P(prevalence): 69/10,000=0.00069 (Kumar 2015)

e= allowable error considered at 0.01 or 1%

n=26.4 individuals per group

Patients, both men and women aged above 18 years and diagnosed with leprosy were included. Patients with other causes of neuropathy such as HIV, thyroid dysfunction or on drugs causing neuropathy such as vincristine and isoniazid were excluded from the study. Informed consent was taken from the 65 participants who were included in the study. Clinical photographs were taken at the same sitting.

Detailed history about the duration of illness, type of leprosy, complaints regarding patch and ulcer, presence of sensory and motor deficits were obtained from all subjects included in the study. For each patient bilateral ulnar, median and common peroneal nerves were palpated by 2 clinicians who reached a consensus regarding characteristics like evidence of thickness, tenderness and presence of abscess were noted. The presence of autonomic changes such as xerosis, change in colour of limbs, evidence of hair loss were observed. Smear status of the patient with regard to bacillary index, presence or absence of

deformity was noted and subsequently graded.

Clinical nerve examination of bilateral ulnar, median and common peroneal nerves for thickness was graded as 0: not thickened, 1: asymmetric thickness, grade 2 or rope like thickness, grade 3 with nodular or beaded thickness. Nerve tenderness was graded as grade 0: no tenderness, grade 1: complained of tenderness when asked, grade 2 category who winced on palpation and grade 3 tenderness who withdrew the limb on palpation which elicited severe tenderness.

All the participants of the study were subjected to an ultrasonographic evaluation of both right ulnar (RU) and left ulnar (LU) at elbow, right (RM) and Left (LM) median nerve at wrist, right (RCP) and left (LCP) common peroneal nerves at neck of fibula using a 10-14 Hz linear transducer probe. The sonologist is unaware of whether the participant has leprosy or is a healthy control. Cross sectional dimensions such as greatest diameter (D1 in mm), Least diameter (D2 in mm), circumference (CIR) (mm) and cross sectional area (CSA) (cm sq.), ratio between D2/D1 was determined to assess whether the shape was more elliptical/rounded. The ulrasonographically visualized thickened nerves were observed for features such as hypoechoicity, loss of fascicular structures, inflammation which appears hypoechoic due to edema, vascularity was looked for using Doppler mode on ultrasound, and fibrosis with septate structures within and around the nerves. The presence or absence of fusiform thickening was looked for using the longitudinal view. In addition the number of nerves found to be thick both clinically and ultrasonographically among the six nerves examined respectively were counted.

Data collected was coded and entered into Microsoft Excel spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS) version 16 for Windows. Descriptive statistics have been used to determine demographic details, spectrum of leprosy, presenting complaints, sensory, motor and autonomic deficits, bacillary index and presence of deformities. Independent students t test and chi square tests were used for comparison of nerve dimensions, circumference, cross sectional area and characteristics such as presence of inflammation, fibrosis, hypoechoicity and loss of fascicles. P value < 0.05 was considered as statistically significant.

Taking into consideration that nerves on the dominant side of the body would be thicker than the other, we have calculated the ΔCSA value for ulnar, median and common peroneal nerve taking the difference in mean CSA for cases and controls. This parameter was initially described by Klauser et al (2011) to enhance the diagnostic accuracy of ultrasound in carpal tunnel syndrome. Receiver operator characteristics were used for the calculation of cut off values along with the sensitivity and specificity of these values for thickness of both right and left ulnar, median and common peroneal nerves respectively.

Results

Among the cases that were recruited 13(37.2%) were aged <30 years, 17(48.5%) patients were aged 31 to 60 years and 5 (14.3%) were aged >60 years. The controls comprised of 16(53.3%) individuals aged between 31-60 years, 11(36.7%) in the <30 year age group and 3(10%) persons aged over 60 years.

Our study showed a male preponderance of 22 (73.3%) among patients and 22 (73.8%) among controls. A p value at 0.931 indicates there is no significant difference in sex distribution in both groups indicating that both cases and controls are sex matched.

The main symptoms of the patients included

presence of ulcer among 8 (22.9%) and hypo-pigmented anaesthetic patch in 27(77.1%). A majority of the cases comprised of the borderline spectrum at 22(62.9%), followed by lepromatous, pure neural and tuberculoid at 6 (17.1%), 4 (11.4%) and 2 (5.7%) respectively. One patient had histoid type of lepromatous leprosy with nodular lesions.

Clinical nerve examination of bilateral ulnar, median and common peroneal nerves (210 nerve points) revealed a total of 86 thickened nerves out of which 47 (55.9%) patients had grade 2 or rope like thickness, 26 (30.3%) with grade one or asymmetric thickness and 13 (14.8%) had nodular or beaded thickness. Among these 86 thickened nerves, 26 (30.8%) nerves had grade 0 or no tenderness, 33 (38.2%) had grade 1 tenderness or complained of tenderness when asked, 16 (19.1%) belonged to grade 2 category who winced on palpation and 11 (11.9%) had grade 3 tenderness and withdrew the limb on palpation which elicited severe tenderness.

Out of 210 nerve points examined though only 86 were found to be clinically thickened, 138 were found to be thickened on ultrasonography. On observing the ultrasonographic features it was found that 115 (83.3%) of the nerves showed focal thickening, 87(63%) nerves showed hypo-echoicity and loss of fascicular architecture, 7(0.05%) nerves revealed features suggestive of inflammation around the nerves, 4(0.03%) and 2(0.01%) nerves showed fusiform thickening longitudinally and fibrosis respectively. (Table 1)

Comparison of the RU between the two groups shows that the smallest and largest diameter is higher in cases and is statistically significant with a p value of <0.001. The RU D2/D1 between the two groups shows a ratio approaching 1 in cases is statistically significant with a p value of 0.015 indicating that thickened nerves are more rounded in shape. The right ulnar circumference and CSA is higher in cases than controls and is statistically significant with a p value of <0.001.

Comparison of the LU between the two groups shows that the smallest and largest diameter is higher in cases and is statistically significant with a p value of 0.029 and <0.001 respectively. The LU D2/D1 between the two groups shows a higher value and ratio approaching 1 in cases with a p value of 0.001 indicating that thickened nerves are more rounded in shape. The left ulnar circumference and CSA is higher in patients than controls and is statistically significant with a p value of <0.001. The Δ CSA value for cases and controls is 0.03 and 0.01 cm^2 respectively for ulnar nerve.

Comparison of the right median between the two groups shows that the smallest and largest diameter is higher in cases and is statistically significant with a p value <0.001 respectively. The RM D2/D1 ratio among cases and controls shows a higher value and ratio approaching 1 in cases but was statistically non significant with a p value of 0.20. The RM circumference and CSA was higher in patients than controls and is statistically significant with a p value of <0.001 and 0.007 respectively.

Comparison of the left median between the two groups shows that the smallest and largest diameter is higher in cases and is statistically significant with a p value of 0.002 and <0.001 respectively. The LM D2/D1 ratio among cases and controls shows a higher value and ratio approaching 1 in cases but is statistically non significant with a p value of 0.05. The LM circumference and CSA is higher in patients than controls and is statistically significant with a p value of <0.001 respectively. The Δ CSA value for cases and controls is 0.03 and 0.01 cm^2 respectively for median nerve.

Table 1 : Demographics and outcome variables of the cases and controls

Variable	parameter	Number of controls (percentage) n=30	Number of cases (percentage) n=35
Age	18-30 yrs	11(36.7%)	13(37.2%)
	31-60 yrs	16(53.3%)	17(48.5%)
	>60 yrs	3(10%)	5(14.3%)
	Total	30(100%)	35(100%)
Sex	Female	8(26.7%)	9(25.7%)
	Male	22(73.3%)	26(73.8%)
	Total	30(100%)	35(100%)
Symptom	ULCER	1(3.3%)	8(22.9%)
	PATCH	0(0%)	27(77.1%)
Deficit	SENSORY	1(3.3%)	26(74.3%)
	MOTOR	0(0%)	15(42.9%)
Clinical spectrum	Tuberculoid		2(5.7%)
	Borderline		22(62.9%)
	Lepromatous		7(19.3%)
	Neural		4(11.4%)
	Total		35(100%)
Grade of thickness	0		0(0%)
	1		26(30.3%)
	2		47(55.9%)
	3		13(14.8%)
	Total		86(100%)
Grade of tenderness	0		26(30.8%)
	1		33(38.2%)
	2		16(19.1%)
	3		11(11.9%)
	Total		86(100%)
Autonomic changes	XEROSIS		23(65.7%)
	HAIRLOSS		16(45.7%)
	CHANGE IN LIMB COLOUR		11(31.4%)
	PERIPHERAL LIMB COOLING		7(20%)
Disability	NO	30(100%)	21(60%)
	YES	0(0%)	14(40%)
	TOTAL	30(100%)	35(100%)
Number of thickened nerves	0	29(96.7%)	1(2.9%)
	1	0(0%)	11(16.9%)

	2	0(0%)	8(12.3%)
	3	0(0%)	8(12.3%)
	4	1(3.3%)	6(9.2%)
	5	0(0%)	1(1.5%)
	6	0(0%)	1(1.5%)
	TOTAL	30(100%)	35(100%)
NUMBER OF THICKENED NERVES ON ULTRASONOGRAPHY	0	30(100%)	0(0%)
	1	0(0%)	2(5.7%)
	2	0(0%)	4(11.4%)
	3	0(0%)	7(20%)
	4	0(0%)	10(28.6%)
	5	0(0%)	5(14.3%)
	6	0(0%)	7(20%)
	TOTAL	30(100%)	35(100%)
NUMBER OF THICKENED NERVES	CLINICAL	4	86
	ULTRASONOGRAPHY	0	138
	CLINICAL	4	86
CHARACTERISTIC	Focal thickening		115(83.3%)
	Hypoechoeic and loss of fascicles		87(63%)
	Inflammation		7(0.05%)
	Fusiform thickening		4(0.03%)
	Fibrosis		2(0.01%)

Comparison of the Right common peroneal nerves between the two groups shows that the smallest and largest diameter is higher in cases and is statistically significant with a p value of <0.001. The RCP D2/D1 between the two groups shows a value higher in the control group and is statistically non significant with a p value of 0.626. The RCP circumference and CSA is higher in patients than controls and is statistically significant with a p value of <0.001 and 0.002 respectively.

Analysing the left common peroneal nerves of the two groups shows that the smallest and largest diameter is higher in cases and is statistically significant with a p value of <0.001. The LCP D2/D1 between the two groups shows a higher value in the patients but is statistically non significant with a p value of 0.586. The LCP circumference and CSA is higher in cases than controls and is statistically significant with a p value of <0.001 and 0.001 respectively. (Table 2) The ΔCSA value for cases and controls is 0.07 and 0.0 cm^2 respectively for common peroneal nerve.

Statistical analysis of receiver operator characteristics was determined using a graphical representation and area under curve was obtained.

Table 2 : Mean dimensions with standard deviation of ultrasonographic measurements of nerve in leprosy cases and controls

Nerve	Side	Mean greatest diameter D1±SD (mm)	Mean smallest diameter D2±SD (mm)	D2/D`1+SD	Mean circumference CIR±SD (mm)	Mean CSA±SD (cm^2)
Right Ulnar	Controls					
	N=30	4.2±0.8	2.1±0.2	0.5±0.1	10.6±1.8	0.06±0.01
	Cases					
	N=35	5.7±1.3	3.6±1.4	0.6±0.1	15.5±4	0.18±0.1
						P value<0.001
Left ulnar	Controls					
	4.8±0.9	2.1±0.4	0.4±0.1	11.8±1.8	0.07±0.01	
	Cases	5.4±1.3	3.3±0.9	0.6±0.2	14.2±3.1	0.15±0.1
						P value<0.001
Right median	Controls	3.9±0.7	2.2±0.4	0.5±0.1	10.1±1.3	0.06±0.01
	Cases	4.7±1.1	2.8±0.8	0.6±0.1	12.1±2.8	0.12±0.1
						P value 0.007
Left median	Controls	4.1±0.5	2.0±0.3	0.5±0.1	10.2±1.0	0.06±0.01
	Cases	4.7±1.0	2.7±0.7	0.6±0.2	12.2±2.6	0.10±0.04
						P value <0.001
Right common peroneal	Controls	3.8±0.6	2.0±0.3	0.5±0.1	9.7±1.3	0.06±0.01
	Cases	5.7±1.8	3.0±0.9	0.5±0.1	14.5±4.8	0.17±0.2
						P value 0.002
Left common peroneal	Controls	3.7±0.6	2.0±0.2	0.5±0.1	9.4±1.3	0.05±0.01
	Cases	5.5±1.9	3.0±1.2	0.6±0.1	14.0±4.9	0.18±0.1
						P value 0.001

Table 3 : The cut off values for nerve CSA for each nerve with sensitivity and specificity for each cut off value

Test Result Variable(s)	CUTOFF VALUES	SENSITIVITY	SPECIFICITY
RU CSA	0.095	88.60%	96.40%
LU CSA	0.085	85.70%	71.40%
	0.1	74.30%	92.90%
RM CSA	0.075	71.40%	67.90%
	0.085	65.70%	92.90%
LM CSA	0.075	74.30%	82.10%
	0.085	65.70%	96.40%
RCP CSA	0.075	88.60%	85.70%
LCP CSA	0.065	91.40%	75.00%
	0.075	77.10%	89.30%

Through our study we have extended this application of receiver operator characteristics to determine the cut off values for nerve thickness for left ulnar, right and left median, right and left common peroneal nerves respectively at 0.08, 0.075, 0.075, 0.075, 0.065 cm^2 respectively with reasonable sensitivity and specificity. The area under each curve was calculated, all of which was above 0.08 which could be considered a good predictor for evidence of nerve thickness. The corresponding cut off value for nerve thickness in each nerve was calculated and tabulated with the sensitivity and specificity percentages for each value as shown in Table 3.

Discussion

The importance of early diagnosis of nerve involvement in leprosy has been emphasized in various studies (Lawande et al 2014). Ascertaining the presence of enlarged nerves clinically can be challenging because of their deeper course between fascial planes. However, high-resolution sonography has been used to demonstrate even subclinical nerve enlargement and inflammation (Jain et al 2009).

On ultrasound examination the normal nerves appeared oval to round with a honey comb pattern representing the nerve fascicles surrounded by a hyperechoeic perineurium (Fig. 1). No signs of inflammation or fibrosis were visualized. On measuring the cross sectional area the highest mean value was obtained for the ulnar nerve when compared to the median and common peroneal nerve. This was similar to findings in a study done by Jain et al (2009).

The superiority of ultrasound in comparison with nerve conduction studies has been highlighted by Elias et al (2009) where it is proved that nerve conduction detects sensory and motor nerve affection which could be normal even in advanced cases of leprosy neuropathy. In this case the nerve has disturbed anatomy with preserved function which can be easily detected using ultrasonography (McLeod et al 1975).

In our study we found that the ΔCSA values

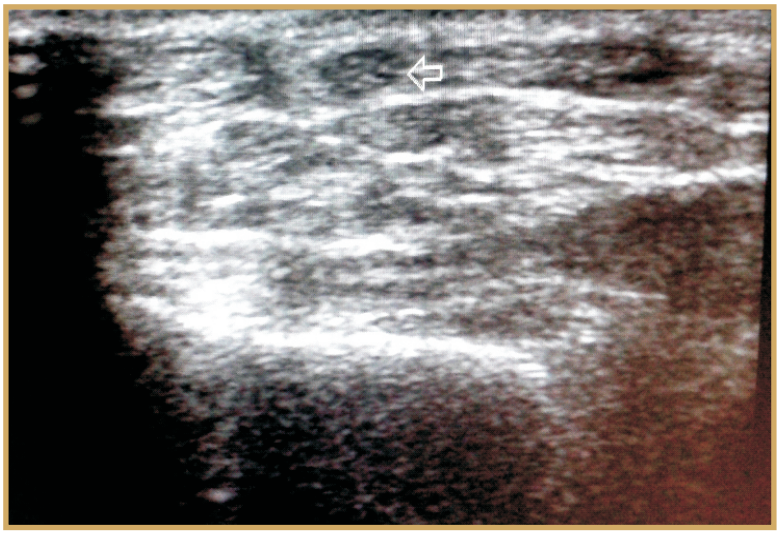

Fig. 1 : Right Ulnar nerve of a healthy volunteer with visible fascicles with CSA 0.07 sq cm

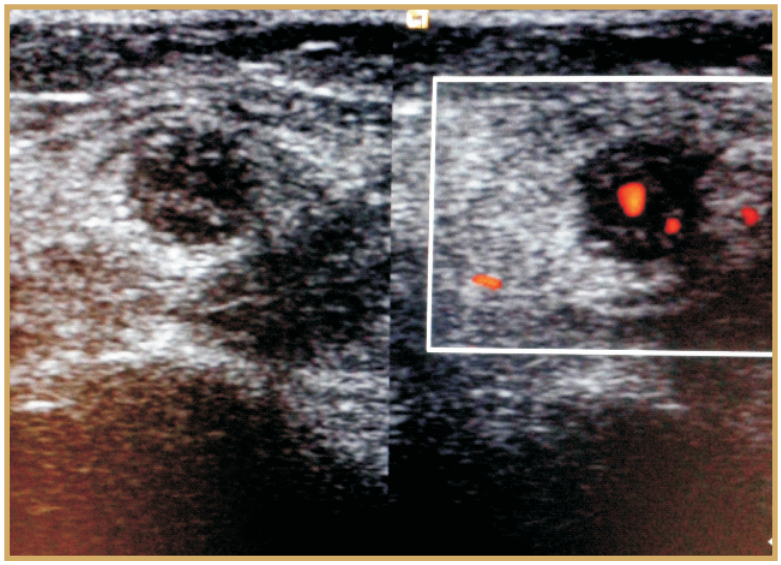

Fig. 2 : Thickened and inflamed Ulnar nerve showing rounded contour, hypoechocity and increased vascular signals on Doppler (inset). CSA 0.14 sq.cm

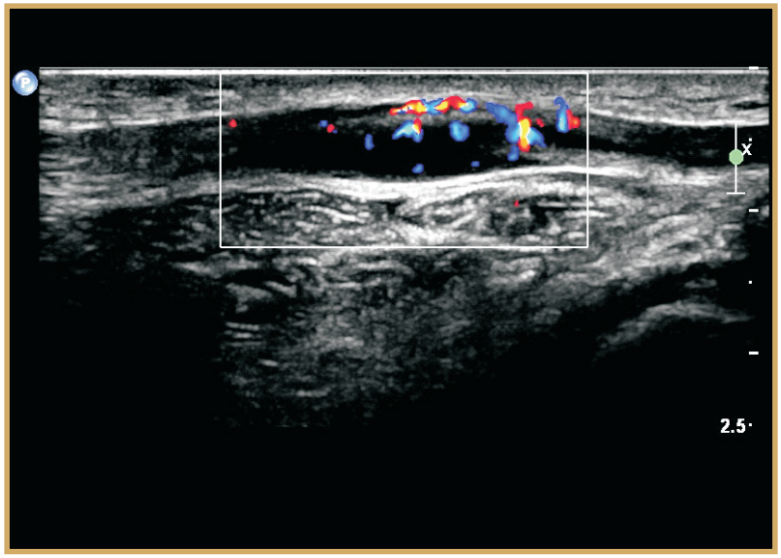

Fig. 3 : Longitudinal view with fusiform enlargement

are higher for patients than controls for ulnar, median and common peroneal nerves which is in accordance with the findings by Elias et al (2009). The most common ultrasonographic finding included focal thickening seen in 115 (83.3%) of the nerves followed by 87 (63%) nerves showing hypoechoicity and loss of fascicular architecture, 7 (0.05%) nerves revealed features suggestive of

inflammation around the nerves, these findings are similar to those seen in a study by Elias J et al (2009) showing focal thickening in 90.5%, hypo-echoic areas in 81%, loss of fascicular pattern in 33% nerves. Another finding noticed in our study includes fibrosis within the hypoechoic areas (Fig. 2) seen in 2 (0.01%) nerves which can be explained to occur as a result of chronic nature of the illness and subsequent to granuloma resolution. Fusiform nerve thickening seen in 4 (0.03%) nerves has been described by Frade et al (2013). (Fig. 3)

The cut off value for ulnar nerve thickness at 9.8 mm^2 was established in another study (Elias et al 2009). This is comparable to the cut off determined in our study at 0.095 cm^2 seen in our study. (Fig. 4)

Thickened nerves appear rounded, thus an attempt was made to determine the ratio between the cross sectional greatest and least diameter. A cross sectional ratio of greatest to least diameter close to one has been noticed in cases than controls, this finding renders the nerve to appear more rounded and has been proved to be statistically significant in both right and left ulnar nerves.

Limitations of this study include lack of a gold standard for comparison of ultrasound as a modality to identify nerve thickening. In our study clinical detection of nerve thickening is the

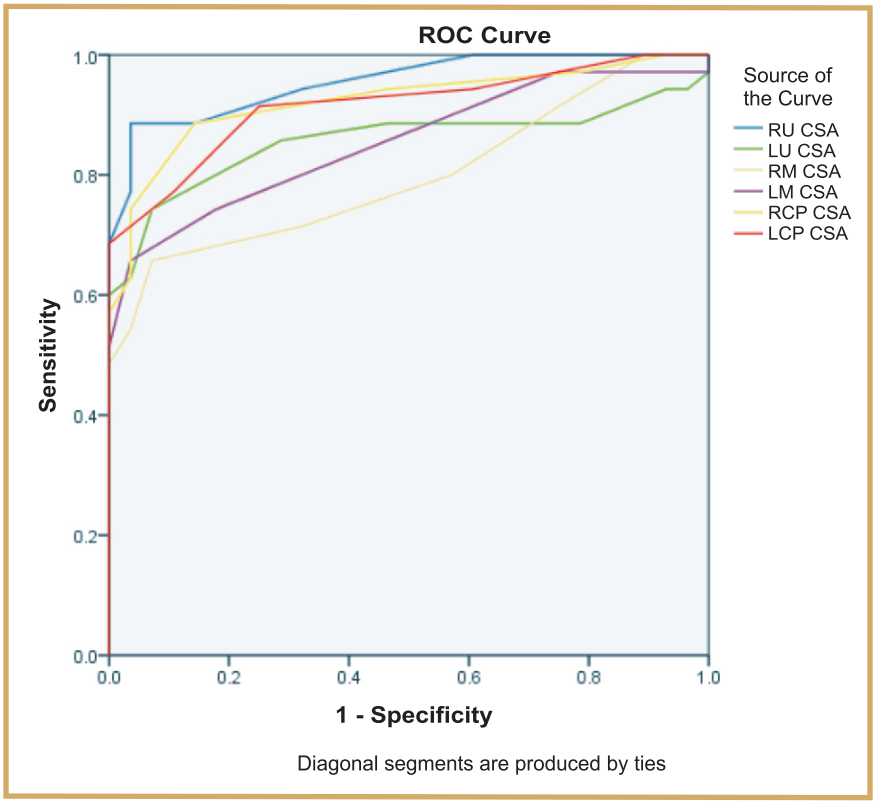

Fig. 4 : Receiver operator curve characteristics for the calculation of cut off values for nerve thickness

deciding factor for enrollment into the study. Although this does not diminish the importance of ultrasound in nerve thickness detection, it is possible that we have missed cases of leprosy with neuropathy that were clinically not appreciated. Following up of the patient for changes in neuropathy following the institution of therapy is also desirable with a larger number of subjects recruited.

Conclusion

One of the hallmark signs of leprosy is nerve enlargement. Evidence from our study indicates that sonographically the thickness is significantly higher in leprosy patients than healthy controls. Ultrasound is a noninvasive and cost effective modality that acts as an effective and objective marker of nerve thickening in leprosy showing increased vascularity, thickness, hypoechoicity and loss of nerve fascicles when compared to clinical examination. It is an important modality in diagnosis of conditions like pure neural Hansen s disease with smear negativity which warrants immediate treatment. A cut off value above 0.08 cm^2 is considered a good predictor of nerve thickness from our study. Establishing this cut off value for nerve thickness and looking for nerve characteristics especially ratio between greatest and least diameter, circumference and cross sectional area provide newer tools to methodically diagnose nerve thickening using ultrasound.

What s new in this study?

- Out of 210 nerve points examined 86 were found to be thickened and 138 were found to be thickened ultrasonographically.
- On ultrasonography most common finding was focal thickening followed by hypoechocity, inflammation around the nerves, fusiform thickening longitudinally and a new finding of fibrosis was noted.
- The right and left ulnar, median and common peroneal nerves showed significant thickening in leprosy patients when compared with healthy controls.
- The ΔCSA values are higher for patients than controls for ulnar, median and common peroneal nerves thus negating the effect of dominant side showing increased nerve size.
- A value above .08 cm^2 is considered a good predictor of nerve thickness.
- The nerve to appear more rounded and has been proved to be statistically significant in both right and left ulnar nerves.

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