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RESEARCH

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# Sonographic evaluation of peripheral nerve involvement in leprosy with electrophysiologic correlation: a cross-sectional study in sub-Himalayan region

Neeti Aggarwal[1], Pooja Thakur[1], Sumala Kapila[1], Shruti Thakur[1*], Anupam Jhobta[1], Sushma Makhaik[1] and Charu Smita Thakur[1]

## Abstract

**Background** Leprosy is an age-old chronic infectious disease with the majority of annual new case detections from South-East Asia. The disease manifestations coupled with the stigma attached to it often creates grave socioeconomic problems. Leprosy is curable and if detected and treated in the early stages can prevent disability. Ultrasonography provides information regarding location and degree of the nerve damage, nerve morphologic alterations, echo texture, fascicular pattern and vascularity. The aim of this study was to study the ultrasonographic features of neuropathy in leprosy with electrophysiologic correlation.

**Results** A total of 34 histopathological proven cases of leprosy were included in this study, which was conducted for 1 year. High-resolution ultrasound (HRUS) of a total of 204 peripheral nerves in these 34 patients, including bilateral ulnar, median and common peroneal nerves, was performed. Cross-sectional areas, nerve diameters, nerve morphology and vascularity were noted and correlated with electrophysiologic study of these nerves. The results showed that all the patients having reduced motor or sensory function [decreased compound muscle action potential (CMAP), decreased compound nerve action potential (SNAP) and increased latency] in ulnar and common peroneal nerves were thickened on HRUS (100% in ulnar and common peroneal nerves) while 92% right median and 89% left median nerves with reduced motor or sensory function showed thickening on HRUS. Also, 5.8% ulnar nerves and 11.7% common peroneal nerves showed thickening on HRUS; however, sensory or motor conduction of these nerves was unaffected on nerve conduction study (NCS). So, a positive correlation was observed for nerve involvement as detected by ultrasonographic findings of nerve hypertrophy and the electrophysiologic study. The most common finding was focal or diffuse nerve thickening. Ulnar nerve was the most commonly thickened nerve in leprosy patients with the most common location of nerve thickening at medial epicondyle.

**Conclusions** Ultrasound and electrophysiologic study of peripheral nerves in leprosy are complimentary to each other in diagnosing leprotic neuropathy.

**Keywords** Leprosy, Peripheral nerves, Ultrasound, Electrophysiologic study

## Background

Leprosy or Hansen's disease is a multisystem disease and its manifestation can vary from an insignificant skin lesion to extensive disease, causing profound disability and disfigurement. No other human disease has a

*Correspondence:
Shruti Thakur
tshruti878@yahoo.in
[1] Department of Radiodiagnosis, Indira Gandhi Medical College and Hospital, Shimla, HP 171001, India

number of handicaps and disproportionate mental suffering as with this disease. The causative bacillus Mycobacterium leprae infects the Schwann cells that surround the nerve fibres and axons [1].

Nerve involvement in leprosy affects sensory, motor and autonomic functions of peripheral nerves. Sensory nerve function impairment (NFI) manifests as altered heat and cold sensitivity, hypoesthesia to anaesthesia leading to neuropathic ulcers, and secondary infection leading to severe deformities [2]. The motor nerve involvement ranges from mild to severe muscle weakness, which may progress to paralysis. The autonomic involvement manifests as decreased sweating with severe dryness and fissuring of the skin [3].

Early diagnosis and initiation of multidrug therapy (MDT) prevents deformities, lowers the grade of disability, lowers the chances of new disability development and increases the chances of recovery from sensory impairments [4]. Early diagnosis of nerve damage in leprosy patients is possible using conduction studies, thermal perception and nerve palpation for thickening**.** All these three modalities are examiner-dependent and require practical training and skills with wide interobserver variability [5]. Electrophysiologic study of peripheral nerves still represents non-invasive gold standard and helps in demonstrating the integrity of nerve function in leprosy. But it does not always allow assessment of the exact location, cause and extent of a nerve lesion. Nerve conduction study (NCS), a part of electrophysiologic study, provides reliable information regarding large myelinated nerve fibres impairment [6]. Electroneurography requires special equipment and skilled technicians and is expensive [7].

Ultrasonography (USG) can explore the affected segment of nerve at multiple sites in single sweep and also helps in diagnosis of compression syndrome. It provides an objective measure of nerve damage and provides information regarding location and degree of nerve damage, morphologic alterations, echotexture, fascicular pattern and vascularity of nerves. A highly correlated finding is a fusiform thickening of peripheral nerves that are generally compromised in leprosy patients, which can be measured by corresponding cross-sectional areas (CSAs) of the affected regions [1, 8]. Ultrasound can also help to guide local injection therapy around the abnormal nerve segment and for performing percutaneous nerve biopsies in atypical or suspected disease [9]. Pure neuritic leprosy, found in Indian subcontinent, does not have dermatological manifestations [10]. However, it can be diagnosed sonologically, which shows raised intra/perineural vascularity or nerve abscess formation.

The median (M), ulnar (U) and common peroneal (CP) nerves represent the most critical peripheral nerves of leprosy patients, which can be assessed by USG. In addition, USG can also demonstrate muscle abnormalities such as atrophy and fat replacement [11].

This study was conducted to determine the reliability of USG of nerves in leprosy patients in early diagnosis so as to reduce the morbidity and disability in these patients. The study involved sonological evaluation of bilateral ulnar nerves, median nerves and common peroneal nerves in leprosy patient to demonstrate peripheral nerves involvement and their electrophysiologic correlation.

## Methods

This cross-sectional prospective study was done in a tertiary institute in sub-Himalayan region for a period of 1 year. A total of 34 diagnosed patients (with 204 peripheral nerves including bilateral ulnar, medial and common peroneal nerves) having histopathologic features suggestive of leprosy, with age more than 10 years and ready to undergo the study, were included. The exclusion criteria were previous history of elbow, wrist or knee trauma, history of peripheral nerve (ulnar, median or common peroneal) surgery, patients with familial neuropathies, systemic lupus erythematosus, alcoholism and any previous peripheral neuropathies as in HIV, thyroid dysfunction or on drugs causing neuropathy such as vincristine and isoniazid. Also, the patients with severe neuritis were excluded temporarily until the neuritis settled down.

A detailed history of patient was taken to know the duration of symptoms, complaints regarding skin patch, ulcer and deformities and histopathological type of leprosy (bacillary index, morphological index). Neurological examination was performed to evaluate for any sensory and motor deficit and for any localizing signs. After explaining the procedure and obtaining the informed consent from the patient, nerve conduction studies (NCS) and high-resolution ultrasound (HRUS) with colour Doppler power imaging (CDPI) of the peripheral nerves were done within a period of 2 days.

### USG imaging acquisition

USG was done by a radiologist having 12 years of experience in general radiology and who was blinded to NCS report. All the sonographic examination sequences were performed (on GE LOGIQ P6 263780509 machine) with a multifrequency (7–10 MHz) electronic real-time linear array transducer. Colour Doppler power imaging was used for assessing increased vascularity in nerves as in cases of leprotic neuritis. Bilateral ulnar, median and common peroneal nerves were identified and scanned in transverse and longitudinal axes. The identification of nerves was based on their echotexture as well as on anatomic landmarks.

Ulnar nerve was assessed throughout its course with major emphasis in three different regions at elbow joint: above the medial epicondyle between triceps brachii and biceps brachii; deep to the cubital tunnel aponeurosis and below the medial epicondyle between flexor carpi ulnaris and flexor digitorum profundus. The maximum nerve enlargement in these three sites was taken as measurement of ulnar nerve at elbow. The other two sites of ulnar nerve measurements were at axilla and at wrist joint. The median nerve was traced along its entire course from axilla to wrist joint where it was followed into the carpal tunnel. At the wrist joint, just deep to the Palmaris longus tendon and flexor retinaculum, lateral to flexor digitorum superficialis (FDS) and flexor digitorum profundus (FDP) tendons and medial to the flexor carpi radialis tendon, median nerve measurement was taken.

With the patient seated and leg flexed at 90°, common peroneal nerve was localized in popliteal fossa at neck of fibula, medial to the biceps femoris muscle, superficially in subcutaneous plane and the measurement was taken at this site.

Cross-sectional area (CSA), echogenicity, fascicular pattern and vascularity of the nerve at the proposed sites of nerve measurements were assessed. CSA was measured by manual trace at inner borders of echogenic rim of epineurium of the peripheral nerves. Cross-sectional dimensions such as greatest diameter (*D*1) in anteroposterior plane, least diameter (*D*2) in mediolateral plane, circumference, CSA and ratio (*D*1/*D*2) were taken to determine whether the shape of the nerve is oval or round [Fig. 1]. The vascularity of all the nerves was interrogated using CDPI to assess any increased blood flow in nerve or epineurium [10, 12, 13] to see whether the nerve is inflamed or fibrosed [14].

The normal sonographic pattern of nerve is hypoechoic, fascicular tubular structures (multiple hypoechoic parallel linear areas) of variable diameters surrounded by varying amounts of interfascicular echogenic tissue (perineurium) and an outer echogenic rim of epineurium forming the border of the nerve. On transverse scans, nerve reveals a honeycomb-like appearance with rounded hypoechoic neuronal fascicles in a hyperechoic background (Fig. 1). A nerve was classified as abnormal if sonographic study showed hypoechoic or hyperechoic foci of focal nerve thickening and loss of fascicular pattern, increased vascularity or collection within the nerve, hypoechoic focal areas (granulomata) and peripheral hyper echogenicity (epineural fibrosis). HFUS was then followed by nerve conduction study of bilateral ulnar, median and common peroneal nerves within a period of 2 days.

#### Neurophysiologic examination

Nerve conduction study was performed by a neurologist who had 8 years of experience and was blinded to USG findings. Motor and sensory nerve conduction studies were done for bilateral ulnar, median and common peroneal nerves in supine position. Latency, conduction velocity and amplitude were assessed. The latency was measured from stimulus artefact to the first negative take off of the composed muscle action potential (CAMP), amplitude was measured from baseline to negative peak with a sensitivity of 500 microV/division and conduction velocity of each interval were evaluated. If any one of the three parameters, i.e. reduced amplitude, reduced conduction velocity and increased latency, was found, it was taken as abnormal. The data so acquired on HRUS and NCS were compared.

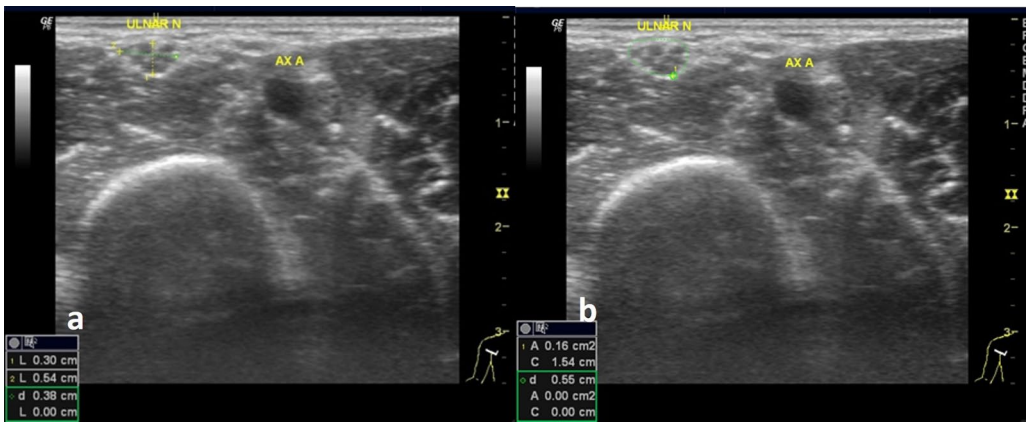



**Fig. 1** Transverse section of normal ulnar nerve at axilla showing typical honey comb pattern: **a** measurement of greatest diameter (*D*1) in anteroposterior plane and least diameter (*D*2) in mediolateral plane and **b** measurement of circumference in cm and cross-sectional area (CSA) in sq.cm of nerve. ULNAR N, ulnar nerve; AX A, axillary artery

*Sample size*: The study was done in a hilly region of Himachal Pradesh, India, where the prevalence of Hansen's disease is 0.56/10,000 [15]. Based on this prevalence, the sample size was calculated with finite population with a precision of 5% and design effect of 1, which came out to be less than 5 subjects as it is an eliminated disease. Hence to further increase the power of the study, it was decided to include all the subjects within the time range (1 year of study period), which was higher (37 patients) than the sample size calculated. Keeping in mind that the apical tertiary care centre would encounter more patients as compared to the other study settings, it was expected to encounter fair number of patients for the study. After excluding patients not fulfilling inclusion and exclusion criteria, finally 34 patients were studied.

### Statistical analyses

Clinical and histopathologic findings, ultrasonological findings and electrophysiologic findings thus obtained were coded and entered in MS excel spreadsheet and analysed using Statistical Package for Social Sciences (SPSS) version 16 for windows. Independent Student's t test and Chi-square tests were used for comparison of nerves dimensions, circumference, cross-sectional area and characteristics such as presence of inflammation, fibrosis, hypo echogenicity, loss of fascicular pattern and increased vascularity. A $p$ value $< 0.05$ was considered statistically significant.

## Results

This study was approved by institutional review board and was conducted over a period of 1 year in a tertiary care institute. A total of 34 histopathologically diagnosed patients (with 204 peripheral nerves) with 25 males and 9 females with an age range from 17 to 76 years (mean age = 40.00 ± 12.54 years) were enrolled in the study. The duration of their symptoms ranged from 1 month to 10 years. Out of these 34 patients, 19 had multibacillary (MB) and 15 had paucibacillary (PB) leprosy. Based on Ridley and Jopling classification [16] of histological typing of leprosy, as shown in Table 1, most of the patients, 15 out of 34 (44.1%) were in lepromatous leprosy (LL) spectrum. Two cases of pure neuritic leprosy showed no skin patches or ulceration clinically; however, there was a loss of nerve function in them.

Nerve conduction studies performed on these 34 patients as shown in Table 2 revealed that common peroneal nerve function was the most common to be impaired closely followed by ulnar nerve. On HRUS, a total of 204 peripheral nerves were assessed, out of which 97 (47%) were found to be thickened which was the most common finding (focal/diffuse). The other USG features are shown in Table 3 and depicted in Fig. 2, and the number of nerves thickened per patient is shown in Table 4. The association of nerve thickening with mean dimensions of ultrasonographic measurements including mean greatest anteroposterior diameter ($D1$), mean least mediolateral diameter ($D2$), $D1/D2$ ratio, circumference and CSA was assessed with significant $P$ values (Table 5).

**Table 1** Disease spectrum of leprosy ($N = 34$)

| Type of leprosy | Number of patients | Percentage |
|---|---|---|
| Pure neuritic BB | 1 | 2.9 |
| BL | 7 | 20.6 |
| BT | 8 | 23.5 |
| LL | 15 | 44.1 |
| Pure neuritic LL | 2 | 5.9 |
| TT | 1 | 2.9 |
| Total | 34 | 100.0 |

BB, mid borderline leprosy; BL, borderline leprosy; BT, borderline tuberculoid leprosy; LL, lepromatous leprosy; TT, tuberculoid leprosy

Ulnar nerve was the most common nerve to be thickened, seen in 47 out of 97 (43.3%) cases [Fig. 3]. Thirty-eight out of 47 thickened ulnar nerves (80.85%) were thickened at and above medial epicondyle with maximum mean CSA of 0.26 sq. cm at medial epicondyle on right side and 0.31sq. cm on left side as described in Table 6. The mean CSA was higher in all the thickened nerves than the non-thickened nerves with significant $P$ values in ulnar and median nerve, and however, it was not significant in bilateral common peroneal nerves (Table 7).

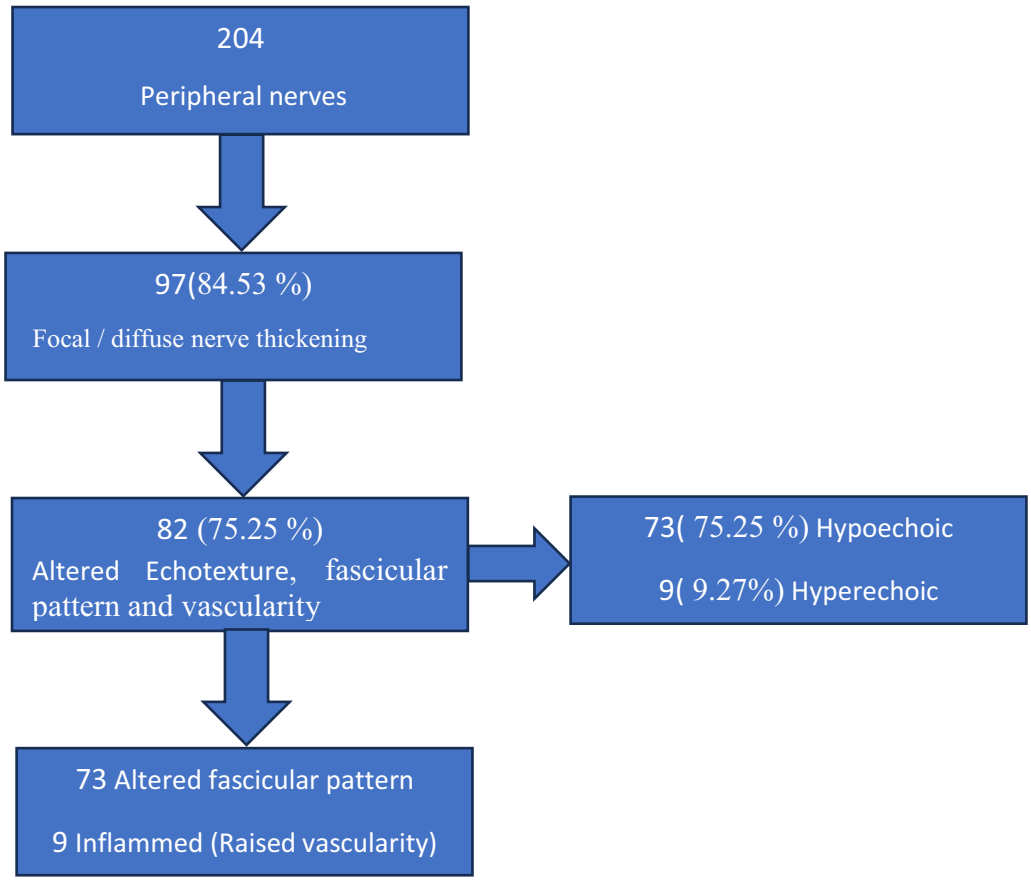
Reduced motor or sensory function on NCS was compared with nerve thickening on HRUS [Figs. 4, 5, 6] as shown in Table 8. All the patients with reduced motor or sensory function [decreased compound muscle action potential (CMAP) and decreased compound nerve action potential (SNAP) and increased latency] in ulnar and common peroneal nerves were thickened on high-resolution ultrasound (HRUS) (100% in ulnar and common peroneal nerves). Reduced motor or sensory function on NCS with thickening on HRUS was seen in 92% right median and 89% left median nerves. However, 5.8% ulnar nerves and 11.7% common peroneal nerves showed thickening on HRUS, even though sensory or motor conduction of these nerves was unaffected on NCS**.** A positive correlation was observed in nerve involvement as detected by ultrasonographic findings of nerve hypertrophy and the electrophysiologic study.

Twenty-four out of 34 cases (70%) showed thickened epineurium [Figs. 2, 3] with mean value of epineurium thickening of 0.79 mm (range 0–1.7 mm) with standard deviation of 0.65. Eleven of these 24 cases (45.8%) were of multibacillary type and 13 (54%) were of paucibacillary type.

**Table 2** Number of patients with normal and abnormal nerve function on nerve conduction study (bilateral ulnar, median and common peroneal nerves)

| Nerve function | Right side (*N* = 34) | Left side (*N* = 34) | Abnormal (both sides) (*N* = 68) | Normal (*N* = 68) |
|---|---|---|---|---|
| Ulnar sensory | 13 (38.2%) | 14 (41.2%) | 27 | 41 |
| Ulnar motor | 11 (32.4%) | 17 (50%) | 28 | 40 |
| Median sensory | 12 (35.3%) | 08 (23.5%) | 20 | 48 |
| Median motor | 06 (17.6%) | 04 (11.7%) | 10 | 58 |
| Common peroneal sensory | 14 (41.2%) | 17 (50%) | 31 | 37 |
| Common peroneal motor | 16 (47%) | 14 (35%) | 30 | 38 |

**Table 3** High-resolution ultrasonographic features of thickened peripheral nerves (bilateral ulnar, median and common peroneal nerves)




## Discussion

The importance of early diagnosis of nerve involvement in leprosy has been emphasized in various studies [17]. Ascertaining the presence of enlarged nerves clinically can be challenging because of their deeper course between fascial planes. However, high-resolution sonography (HRUS) has been used to demonstrate even subclinical nerve enlargement and inflammation [10]. Regional lymphadenopathy (LAP) such as axillary, epicondylar and trochlear can also be assessed in patients with leprae reactions.

Leprotic neuropathy can occur in any age group of leprosy affected patients. In our study, majority of patients were in the age group of 31–40 years (29%) with a male preponderance constituting 73.5%. In a study done by Ashwini et al. [14], majority of patients (17 patients constituting 48.5%) were < 30 years of age with a male preponderance of 73.3% among cases and 73.8% among

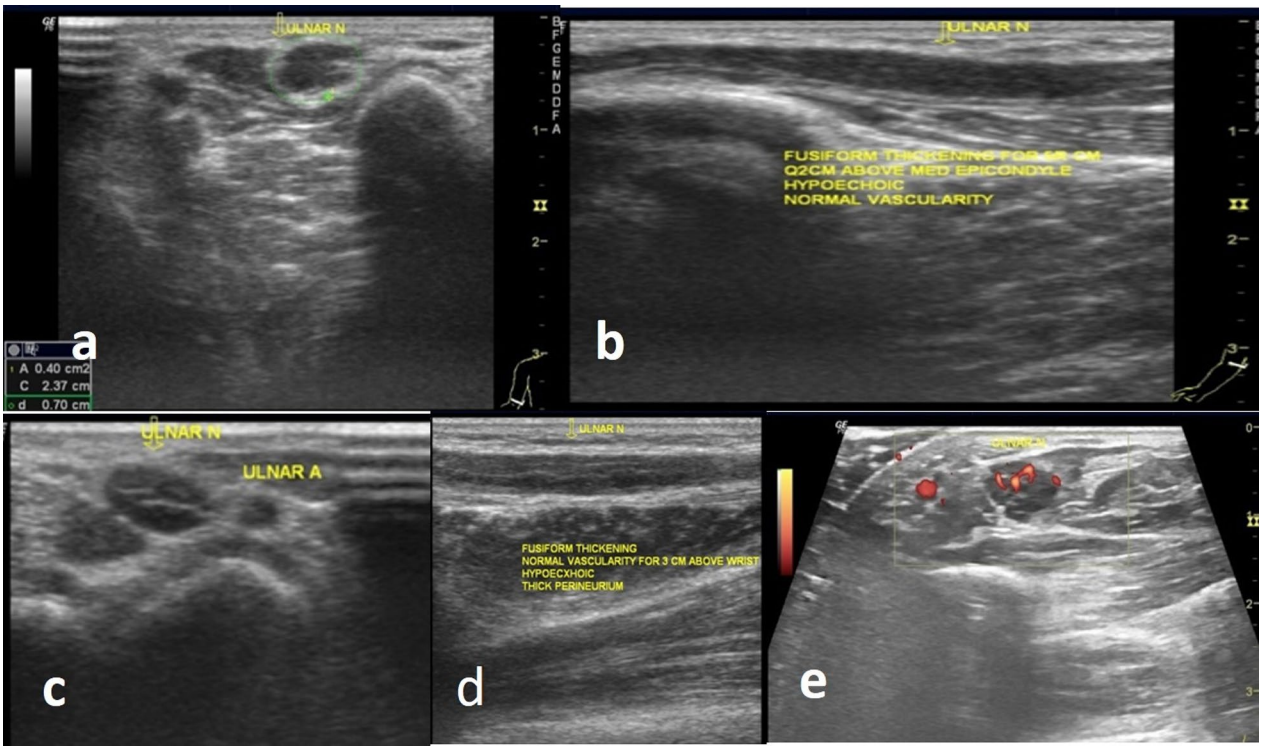



**Fig. 2** A 56-year-old male with pure neuritic LL and severe type 1 reaction showing right ulnar hypertrophic neuropathy and left ulnar neuritis: **a** transverse HRUS shows rounded enlarged right ulnar nerve above medial epicondyle with CSA of 0.40 sq. cm, **b** longitudinal section shows focal fusiform thickening of right ulnar nerve above medial epicondyle with hypo echogenicity and loss of fascicular pattern, **c** transverse HRUS shows rounded right ulnar nerve at wrist, **d** longitudinal section shows thickened hypoechoic right ulnar nerve with thickened epineurium and perineurium at wrist and **e** transverse section left ulnar nerve shows raised intra- and epineural vascularity on CDPI. ULNAR N, ulnar nerve; ULNAR A, ulnar artery

**Table 4** Number of thickened nerves on ultrasound per patient ($N=34$)

| Number of thickened nerves on ultrasound per patient | Number of patients | Percentage |
|---|---|---|
| 0 | 4 | 12 |
| 1 | 5 | 14 |
| 2 | 7 | 20 |
| 3 | 2 | 5.8 |
| 4 | 11 | 32 |
| 5 | 2 | 5.8 |
| 6 | 3 | 8.8 |

controls. So, these findings were consistent with our study.

In our study, we found that nerve dimensions, i.e. maximum AP diameter ($D1$), minimum ML diameter ($D2$), circumference and cross-sectional area (CSA), were significantly greater in all leprosy patients compared with set of reference values reported by Cartwright et al. [18]. The $D1/D2$ of nerves showing hypertrophy was closer to 1 as compared to non-affected nerves that showed $D1/D2 < 1$, suggesting the affected nerves tend to be rounder as compared to non-affected nerves, which tend to be oval on transverse imaging. The most common finding in affected nerves in our study was focal or diffuse nerve thickening seen in 100% of affected nerves followed by altered fascicular pattern and echotexture of nerves (75% nerves were hypoechoic and 9% nerves were hyperechoic). Inflammation around the nerves was seen in 9.27%. In a previous study done by Elias et al. [1], 90.5% of cases had focal thickening, 81% had focal hypoechoic areas, and 4.7% had an ulnar nerve focal hyperechoic area. In another study done by Ashwini et al. [14], 83.3% of the nerves showed focal thickening, 63% nerves showed hypo echogenicity and 0.05% nerves revealed features suggestive of inflammation around the nerves. So, the results in our study were almost consistent with the above-mentioned studies. This also reinforces the diagnostic importance of focal nerve thickening for detection of peripheral neuropathy for disease detection. HRUS also demonstrates early haemodynamic changes in the nerve progressing to develop leprae reaction which could

**Table 5** Association of nerve thickening with mean dimensions of ultrasonographic measurements of peripheral nerves (bilateral ulnar, median and common peroneal nerves)

| Nerve | Nerve thickening | *D*1 (cm) | *D*2 (cm) | *D*1/*D*2 | Circumference (cm) | CSA (Sq. cm) | *P* value |
|---|---|---|---|---|---|---|---|
| Right ulnar nerve | Absent | 0.48 | 0.65 | 0.74 | 1.506 | 0.16 | 0.001 (S) |
| | Present | 0.71 | 0.86 | 0.82 | 2.22 | 0.33 | |
| Left ulnar nerve | Absent | 0.44 | 0.61 | 0.73 | 1.402 | 0.12 | 0.005 (S) |
| | Present | 0.708 | 0.88 | 0.79 | 2.18 | 0.401 | |
| Right median nerve | Absent | 0.47 | 0.608 | 0.77 | 1.36 | 0.17 | 0.001 (S) |
| | Present | 0.71 | 0.87 | 0.81 | 2.12 | 0.301 | |
| Left median nerve | Absent | 0.47 | 0.56 | 0.83 | 1.33 | 0.16 | 0.004 (S) |
| | Present | 0.72 | 0.87 | 0.82 | 2.17 | 0.34 | |
| Right common peroneal nerve | Absent | 0.43 | 0.56 | 0.77 | 1.25 | 0.21 | 0.001 (S) |
| | Present | 0.69 | 0.83 | 0.85 | 1.93 | 0.26 | |
| Left common peroneal nerve | Absent | 0.55 | 0.63 | 0.95 | 1.57 | 0.23 | 0.006 (S) |
| | Present | 0.6006 | 0.79 | 0.75 | 1.86 | 0.28 | |

*D*1: mean greatest anteroposterior diameter; *D*2: mean least mediolateral diameter; CSA: cross sectional area

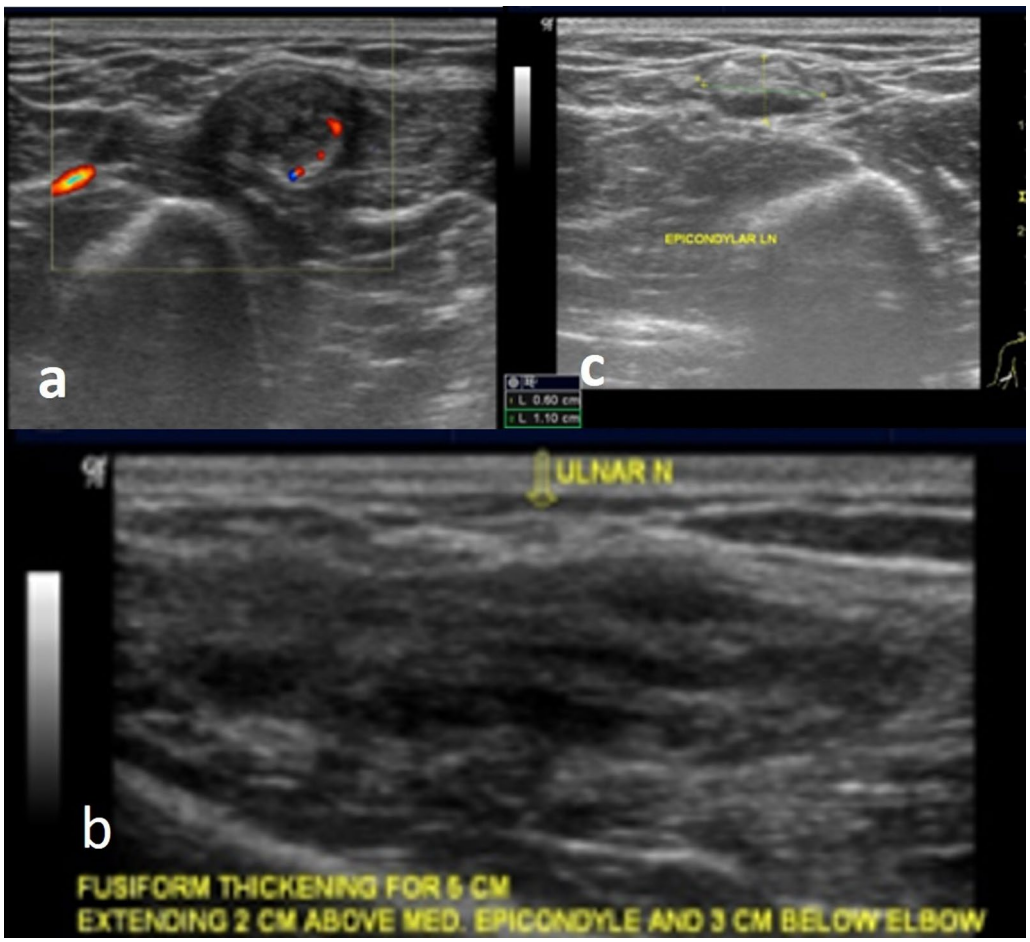



**Fig. 3** A 41-year-old male with LL of 10 years of duration with right ulnar neurohypertrophy and neuritis: **a** transverse section at level of medial epicondyle depicts thickened epineurium with increased intra and epineural vascularity on CDPI, **b** longitudinal section shows focal fusiform thickening, hypoechoic nerve with loss of fascicular pattern, **c** transverse section shows right epicondylar lymph node measuring 6 mm in short axis. ULNAR N, ulnar nerve; EPICONDYLAR LN, epicondylar lymph node

**Table 6** Mean cross-sectional area (CSA) (sq. cm) for bilateral ulnar nerves at axilla, at medial epicondyle and at wrist

| Ulnar nerve | Right | | Left | |
|---|---|---|---|---|
| | Mean CSA (sq. cm) | Std. deviation | Mean CSA (sq. cm) | Std. deviation |
| At axilla | 0.1279 | 0.09194 | 0.1262 | 0.05810 |
| At medial epicondyle | 0.2606 | 0.18254 | 0.3106 | 0.28265 |
| At wrist | 0.1647 | 0.24996 | 0.1549 | 0.20572 |

be useful once standardized, as an early sign to alert the physician leprologist to start corticosteroid therapy [19].

In this study, we studied the correlation between electrophysiological and sonographic findings of bilateral upper and lower limb nerves and observed that 100% cases with abnormal ulnar and common peroneal nerves function showed thickening on HRUS. Eight per cent of right median and 11% of left median nerves with reduced motor or sensory function showed no thickening on HRUS. A study done by Elias et al. [1] showed that 9.5% cases (2 patients) had abnormal NCS findings with normal sonographic findings, again consistent with our study.

On measuring the cross-sectional area, the highest mean value was obtained for the ulnar nerve (0.23 sq. cm in right and 0.22 sq. cm in left) when compared to the median (0.21 sq. cm in right and 0.19 sq. cm in left) and common peroneal nerve (0.21sq. cm in both right and left). In a study done by Ashwini et al. [14], the highest mean cross-sectional area obtained was 0.18 sq. cm and 0.15 sq. cm for right and left ulnar nerves, 0.12 sq. cm and 0.10 sq. cm for right and left median nerves and 0.17 sq. cm and 0.18 sq. cm for right and left common peroneal nerves, respectively. The mean CSA in both studies was higher in ulnar nerve as compared to peroneal nerves.

Ulnar nerve was the most commonly thickened nerve in Leprosy in our study constituting 43.3%, followed by common peroneal nerve (37%) and median nerve (19.6%). Madhusudan et al. [20] showed ulnar nerve as the most thickened peripheral nerve in 35% cases. In our study, 80.85% of thickened ulnar nerves were seen at and above medial epicondyle. In a study done by Elias et al. [1], ulnar nerve thickening as evaluated by sonography showed a tendency to be more severe in the area above the medial epicondyle. In another study done by Dubey et al. [21], 54% cases showed ulnar nerve thickening at elbow in leprosy patients. Thickened epineurium was seen in 24 (70%) cases in our study. A study done by Madhusudan et al. [20] showed thickened epineurium in 3.9% cases. The more percentage in our study can be explained due to long duration of disease in some of our patients. Two cases of pure neuritic leprosy (one pure neuritic LL, one pure neuritic BB) showed no skin patches or ulceration clinically; however, there was loss of nerve function. On HRUS, hypertrophy of various upper and lower limb peripheral nerves was seen in these cases. One of these patients was in severe type 1 lepra reaction. One patient with perineural granuloma formation was also seen in our study.

On HRUS, 5.8% ulnar nerves and 11.7% common peroneal nerves showed thickening; however, no alteration in sensory or motor conduction of these nerves was seen on NCS. In a previous study done by Elias et al. [1], sonographic abnormalities were found in three patients with normal electrophysiologic findings. The superiority of ultrasound over nerve conduction studies has been highlighted in this study in which it is proved that nerve conduction studies may be normal even in

**Table 7** Association between nerve thickening and mean cross-sectional area (CSA) ($N=34$)

| Nerve | Nerve thickening | Mean CSA (sq. cm) | Standard deviation | *P* value |
|---|---|---|---|---|
| Right ulnar nerve thickening | Absent | 0.1256 | 0.07859 | 0.01 (S) |
| | Present | 0.2309 | 0.15935 | |
| Left ulnar nerve thickening | Absent | 0.1403 | 0.11858 | 0.01 (S) |
| | Present | 0.2245 | 0.11461 | |
| Right median nerve thickening | Absent | 0.1761 | 0.11773 | 0.01 (S) |
| | Present | 0.2118 | 0.12818 | |
| Left median nerve thickening | Absent | 0.1638 | 0.11092 | 0.01 (S) |
| | Present | 0.1938 | 0.12760 | |
| Right common peroneal nerve thickening | Absent | 0.1214 | 0.11099 | 0.47 |
| | Present | 0.2175 | 0.12423 | |
| Left common peroneal nerve thickening | Absent | 0.1294 | 0.22558 | 0.6 |
| | Present | 0.2156 | 0.21580 | |

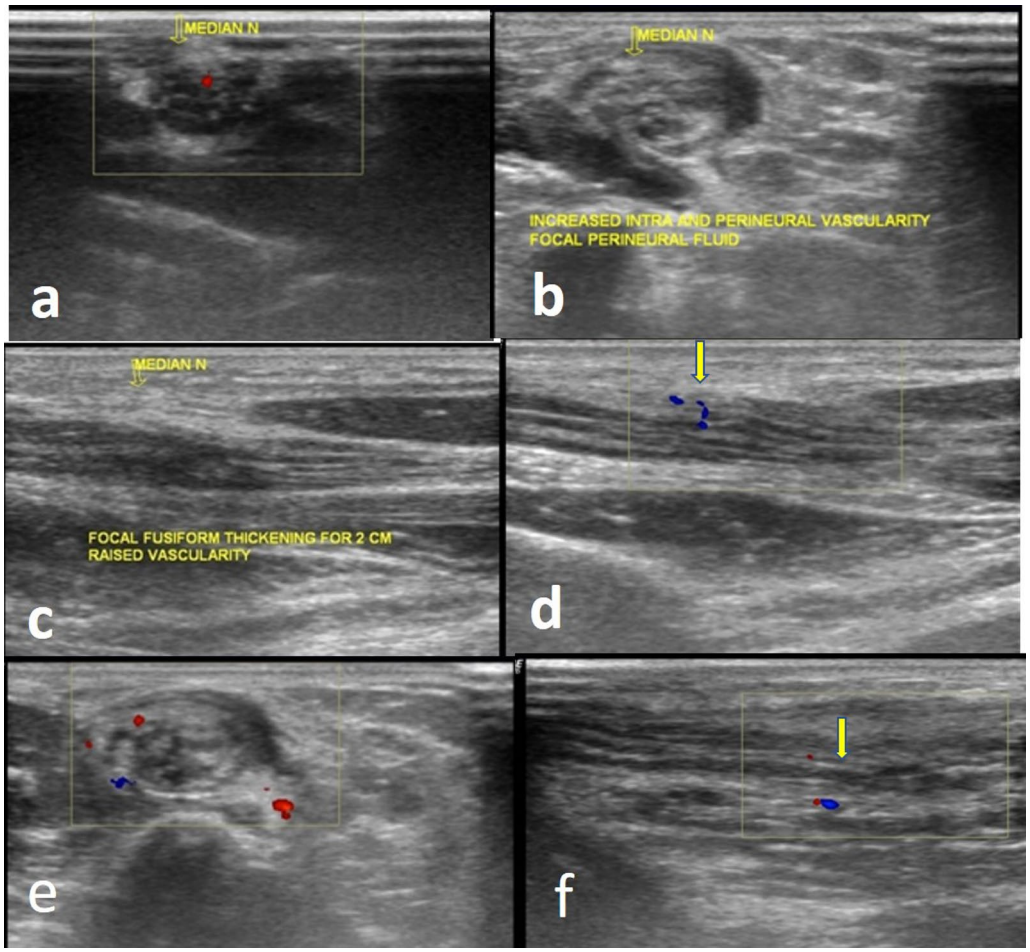



**Fig. 4** A 53-year-old female with LL of 4 years of duration showing bilateral median and left ulnar neurohypertrophy with neuritis and granuloma: **a** Transverse section shows rounded hypoechoic right median nerve at wrist with loss of fascicular pattern and raised intraneural vascularity, **b** transverse section shows thickened hypoechoic right median nerve with partial loss of fascicular pattern and perineural granuloma formation, **c**, **d** longitudinal section shows focal fusiform thickening of left median nerve in forearm with raised vascularity, **e** transverse section shows rounded, and **f** longitudinal section shows thickened left ulnar nerve above medial epicondyle with altered echogenic areas and increased vascularity. MEDIAN N, median nerve

advanced cases of leprosy neuropathy. In such cases, the nerve has disturbed anatomy with preserved function, which can be easily detected using ultrasonography [22]. This also indicates that HRUS may be useful for evaluating nerve anatomy in asymptomatic household contacts of patients with leprosy and predicting the neuropathy prior to nerve conduction studies.

Therefore, it is of no doubt that HRUS is accepted as a useful tool in the diagnosis of primary neuritic leprosy [10]. Using this tool can help early identification of abnormal nerve structure. Nerve involvement if diagnosed in time may be reversible with adequate treatment [23]. Our study had its limitations. It was a study conducted on 34 patients and the results need to be interpreted in a larger study for validation.

## Conclusions

High-resolution ultrasound is a non-invasive and cost-effective tool that gives significant information on peripheral nerve morphology and its vascularity and this adds a whole new dimension in diagnosing leprosy particularly pure neuritic type. Ulnar nerve is the most commonly affected nerve in Leprosy; the most common location of nerve thickening being at and above the medial epicondyle in arm. Though electrophysiological nerve study is gold standard for detection of nerve function impairment in leprosy, ultrasound is better for localization of focal neural thickening and for guiding neural biopsy.

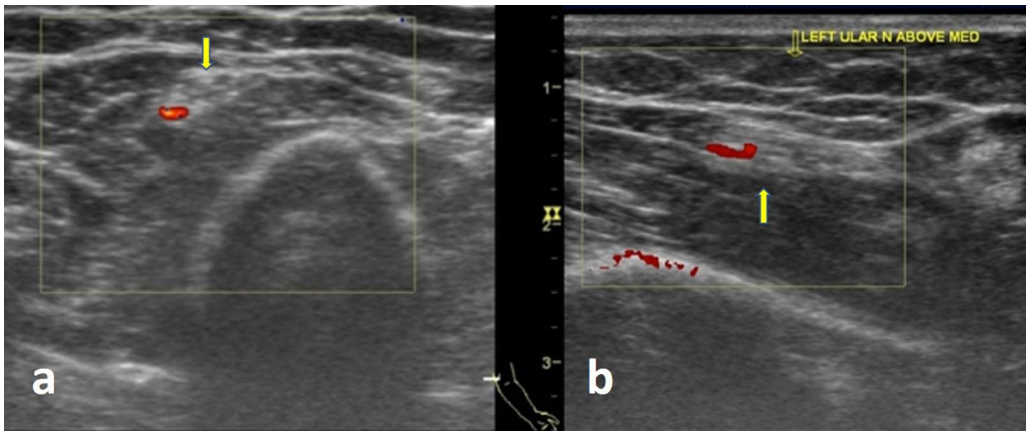



**Fig. 5** A 40-year-old female with BL of duration 2 months with left ulnar nerve hypertrophy and neuritis: **a** transverse section and **b** longitudinal section show echogenic areas within the nerve and increased epineural vascularity of left ulnar nerve (arrow) on CDPI just above medial epicondyle. MED, medial epicondyle

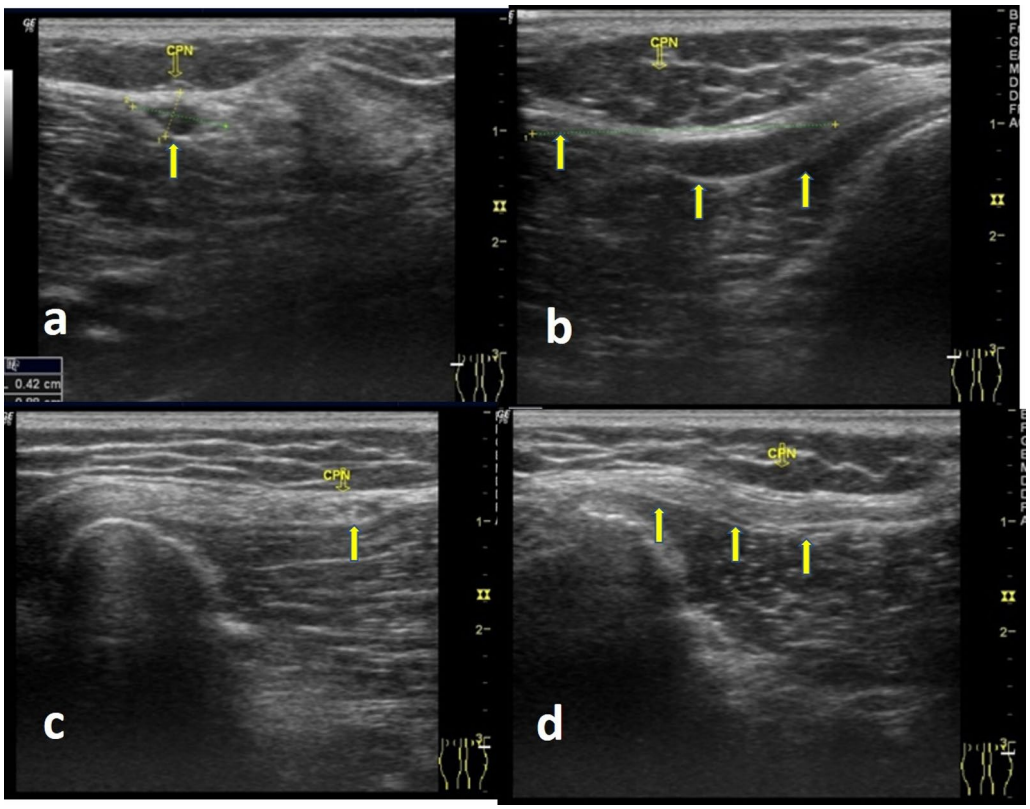



**Fig. 6** A 27-year-old female with BT to BL leprosy of duration 1 month with bilateral common peroneal nerves thickening and normal nerve conduction study: **a** transverse section shows focal rounded right common peroneal nerve (arrow), **b** longitudinal section shows focal fusiform thickening of right common peroneal nerve with hypoechogenicity and loss of fascicular pattern (arrows), **c** transverse section shows focal rounded left common peroneal nerve (arrow), **d** longitudinal section shows focal fusiform hyperechoic thickening of left common peroneal nerve (arrows), with loss of fascicular pattern and thickened epineurium (1.3 mm)

**Table 8** Correlation of peripheral nerve thickening on HRUS and nerve conduction study (NCS)

| | Right ulnar nerve | Left ulnar nerve | Right median nerve | Left median nerve | Right common peroneal nerve | Left common peroneal nerve |
|---|---|---|---|---|---|---|
| Number of nerves with impaired NCS | 19 | 19 | 12 | 9 | 16 | 12 |
| Number of nerves showing sonographic thickening | 19 | 23 | 11 | 8 | 20 | 16 |
| Percentage (no. of thickened nerves with impaired function on NCS) | 100 | 100 | 92 | 89 | 100 | 100 |

**Abbreviations**

| | |
|---|---|
| AFB | Acid fast bacilli |
| BI | Bacteriological index |
| BL | Borderline leprosy |
| BT | Borderline tuberculoid |
| CDPI | Colour Doppler power imaging |
| FDS | Flexor digitorum superficialis |
| FDP | Flexor digitorum profundus |
| LL | Lepromatous leprosy |
| MDT | Multidrug therapy |
| MI | Morphological index |
| NFI | Nerve function impairment |
| NCS | Nerve conduction study |
| TT | Tuberculoid leprosy |
| USG | Ultrasonography |
| HRUS | High-resolution ultrasonography |

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**Author contributions**
Study concepts and design were done by NA, PT and SK. Literature research was done by PT and ST. Clinical studies were carried out by NA and PT. Data analysis were done by NA, PT and SK. Manuscript preparation was done by ST, CT and SK. Manuscript editing was done by NA, AJ and SM. All authors read and approved the final manuscript.

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## Declarations

**Ethics approval and consent to participate**
This study was approved by the ethical review board of this institution "Indira Gandhi Medical College and Hospital, Shimla, HP, India" and followed the Declaration of Helsinki. All patients agreed to participate in the study and provided written informed consent.

**Consent for publication**
Written informed consent was taken from the patients.

**Competing interests**
The authors declare that they have no competing interests.

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