High resolution sonographic examination:  
a newer technique to study ulnar nerve  
neuropathy in leprosy

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Summary
Objectives: A prospective case control study was conducted to calculate normal 
dimensions of ulnar nerve and study the size, echotexture and morphologic alterations 
in ulnar nerve in patients with leprosy.
Methods: The study group included 48 patients diagnosed with leprosy on basis of 
clinical, bacteriologic and/or histopathologic evaluation. Sonographic measurements 
were taken at 3 levels around elbow. The morphology and vascularity were also 
studied. Control group consisted of 60 clinically normal ulnar nerves, on which 
ultrasound was performed to calculate normal parameters. 96 Ulnar nerves were 
independently evaluated clinically and on ultrasound. The mean cross sectional area 
and diameters (both antero-posterior and mediolateral) of controls at all three levels 
were calculated. The normal sonographic dimensions of ulnar nerve were calculated 
based on Mean ± 2SE and beyond the upper limit of normal was considered enlarged 
on ultrasound. Statistical analysis was done using SSPS version 17.0.
Results: The dimensions of ulnar nerve were significantly larger in leprosy group 
for all levels (P value < 0.001). Sonographic abnormalities included hypoechoic 
areas (61.45%), loss of fascicular pattern (same 61.45%) and focal hyperechoic areas 
(48.95%). 37.5% of nerves (6 out of 16) with clinical evidence of reaction showed 
endoneural vascularity.
Conclusions: We conclude that by detecting enlargement and/or morphologic 
alterations of ulnar nerve, sonography can objectively determine involvement of 
ulnar neuropathy in leprosy.

Keywords: Nerve, Leprosy, Sonography
Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* primarily affecting peripheral nerves.\(^1\) This disease of low infectivity is still prevalent in many parts of the world, mostly in developing countries of Asia, Africa and Latin America.\(^2\) India is responsible for the highest disease burden (with a registered prevalence of 91,743 in 2012) and with 4,650 new patients having Grade II deformity.\(^3\) Early case detection and treatment remain the key strategies to decrease disease load, reduce the risk of disease transmission in the community and prevent deformities due to leprous neuritis.

Due to its affinity for peripheral nerves, neuropathy is the cardinal feature of leprosy. Nerves that are predominantly involved include the ulnar nerve (UN), median nerve, lateral popliteal nerve, posterior tibial and greater auricular nerve, with or without skin lesions.

The presence and degree of nerve involvement is usually evaluated by clinical assessment and by nerve biopsy at times when there is isolated nerve involvement. Nerve conduction studies often fail to attribute leprosy as the cause of neuropathy with certainty. Nerve biopsy is an invasive procedure and its histological interpretation needs specific skills.\(^4\) Also due to the risk of worsening the neurological deficit, a biopsy cannot be performed on nerves having a motor component, such as the ulnar nerve.\(^5\) Clinical assessment of the functional impairment of peripheral nerves may be inadequate and inaccurate as clinical evidence of neuropathy may appear late even in the presence of nerve damage.\(^6\) Immunocytochemical techniques, though helpful in evaluating nerve damage, are limited by their cost and availability.

Nerve involvement may be precipitated during lepra reactions (both Type I and Type 2 reactions) in 15–50% of patients during the course of the disease or after the completion of multidrug therapy. Careful nerve evaluation is essential to detect recent nerve function impairment of the affected nerves during each episode of reaction. The nerve involvement by leprosy reactions, if recognised and promptly treated with steroids can be reversible.

The role of non-invasive imaging techniques, including ultrasonography (USG) and magnetic resonance imaging (MRI) is under exploration and can serve as an important tool to identify both silent and active nerve involvement, thereby preventing deformity and disability.\(^7\)

The superficial location of the ulnar nerves facilitates their evaluation by High Resolution USG, and the nerve can be probed along its length in both static and dynamic states.

The present study was conducted with the following aims:

(a) To calculate the normal dimensions of ulnar nerve at three levels around the elbow.
(b) To study the morphologic alterations on high resolution sonography in ulnar nerve neuropathy of leprosy.
(c) To study the role of Colour Doppler flow imaging in ulnar neuropathy of leprosy.

Materials and Methods

This prospective case control study was approved by the institutional ethical board and conducted over a period of 18 months in the departments of Dermatology and Radiology. After obtaining written informed consent, 48 leprosy patients, diagnosed on the basis of clinical, bacteriologic and/or histopathologic evaluation and classified as per Ridley-Jopling criteria, constituted the study group. Patients were either untreated or on antileprosy
treatment for less than 3 months duration. Patients with a previous history of mechanical trauma or surgery around the region of the elbow were excluded.

Thirty normal healthy individuals without any clinical evidence or risk factor of developing peripheral neuropathy constituted the control group. All study subjects with associated neurological disorders such as familial neuropathies, or having a systemic disorder known to cause peripheral neuropathy, including alcoholism, diabetes, amyloidosis, and neurofibromatosis, were excluded.

Therefore, 96 ulnar nerves in leprosy patients and 60 normal ulnar nerves were evaluated, both clinically and on high resolution US.

All leprosy patients were examined clinically for any skin lesions and both ulnar nerves were assessed for neurological (sensory or motor) impairment. The presence of any thickening on palpation was graded as follows:8

- 0- Nerve not thicker than contra-lateral nerve, with no abnormal sensation/neurological involvement.
- 1- Nerve thicker than contra-lateral nerve.
- 2- Thickening of the affected nerve was rope like and diffuse.
- 3- Thickened nerve which appears beaded/nodular or with abscess formation.

Thereafter a detailed sonographic assessment of the ulnar nerves in both control and study groups was carried out by an experienced radiologist blinded to all the clinical details. The radiologist was unaware whether the person being examined was a leprosy patient or a healthy control.

High Resolution Real – Time Sonographic examination of both ulnar nerves was done using HDI 5000 scanner (Philips) equipped with a phased array broadband 5–12 MHz linear transducer. The patient was examined in the supine position for the right nerve while keeping his right arm slightly abducted with 30 degree of flexion at the elbow. For examination of the left nerve, the patient was turned to the prone position and the left arm was slightly abducted with 30 degree of flexion. USG criteria for nerve identification were based on analysis of their echo pattern as well as on detection of anatomic landmarks. (Figures 1 and 2). All the abnormal findings were recorded on a pre-designed form.

On the gray scale imaging, the measurement of size [Cross sectional area (CSA)] of the ulnar nerve was done by the radiologist at three regions:

1. 4 cms above the medial epicondyle between triceps brachii and biceps brachii.
2. Deep to cubital tunnel.
3. Below the medial epicondyle between flexor carpi ulnaris and flexor digitorum profundus.

The dimensions were taken with electronic calipers placed inside the echogenic epineurium. Normal ranges of the dimensions were calculated using Mean ± 2 SE of the values in control group. All nerves lying above the calculated upper limit were considered to be thickened.8

The region of focal thickening and the maximum diameter in case of diffuse nerve thickening were also recorded (Figures 3 and 4).

Other morphological parameters recorded at the level above the medial epicondyle were:

- Presence of any focal hyperechoic areas within the nerve (Figure 5).
- Presence of hypoechoic areas within the nerve (Figure 4).
Figure 1. Longitudinal view showing the normal ulnar nerve composed of hypoechoic parallel tissue separated by echogenic bands of epineurium (thin arrow).

Figure 2. Transverse view showing normal speckled fascicular pattern (thin arrow) of ulnar nerve 2 cms below medial epicondyle surrounded by hyperechoic perineurium (thick arrow).
Loss of fascicular pattern (Figure 4).

- Endoneural and perineural vascularity on Colour Doppler study. The presence of blood flow signals in the perineural plexus or intrafascicular vessels indicated hypervascularity of the nerve (Figure 6).

The analysis was done in SSPS version 17.0. Differences between controls and cases for various quantitative parameters were obtained by unpaired ‘t’ test and ANOVA. Frequency distribution of morphological changes was also obtained. Fisher’s exact test was used to calculate the significance of differences in morphological pattern. *P* value <0.05 was considered significant.

**Figure 3.** Transverse view shows thickened ulnar nerve with measurements made within the hyperechoic boundary. AP diameter and ML diameter are depicted by ‘x’ and ‘ ’ respectively.

**Figure 4.** Transverse view with cross sectional area of 0.25 cm², loss of fascicular architecture and focal hypoechoic areas.
Results

The mean age of the control group was 38 years and the range was 10–80 years. Thirteen individuals were male and 17 were female. No clinical thickening or tenderness of the ulnar nerve or abnormal neurological examination was present in this group.

In the control group, the mean CSA of the ulnar nerve was $4.08 \pm 0.14 \text{cm}^2$, $4.55 \pm 0.02 \text{cm}^2$, $4.00 \pm 0.13 \text{cm}^2$ above the level of the epicondyle, at the cubital tunnel and

**Figure 5.** Focal Hyperechoic areas in a thickened ulnar nerve as marked by + and x cursors.

**Figure 6.** Colour Doppler image showing increased endoneural and perineural vascularity as shown by the Doppler signal in this case with Type 1 Reaction.
below the medial epicondyle, respectively. Ulnar nerves appeared as oval or round with occasional internal punctuate echoes on transverse scans. On longitudinal scanning, the ulnar nerve was seen as a hypoechoic tubular structure with parallel linear internal echoes. The epineurium and peri-neurium were uniformly hyperechoic with an absence of abnormal epi- and endoneural blood flow signals on Colour Doppler imaging. All the nerves displayed normal echotexture without any morphological alteration. The echotexture of the normal ulnar nerve was appreciated with difficulty in the region of cubital tunnel due to the problem of anisotropy and its position in a bony canal. There was no significant gender related difference in these measurements.

Forty eight adult leprosy patients with 96 ulnar nerves underwent both clinical and sonographic examination. The mean age of patients was 40 years, 40 patients were male and eight were female (Table 1).

The patients were classified according to the Ridley-Jopling classification. Four (8·3%) patients were classified as having pure neuritic form of leprosy.

As already described, sensory symptoms are a common finding in the study group as it is usually the first neural manifestation. Ten patients (20 nerves) presented without any sign of neural damage (sensory or motor symptoms) on clinical examination but thickening was observed in 18/20 (90%) according to USG criteria. Thus, a sonographic scan could detect an abnormal ulnar nerve in the absence of any clinical or neurological manifestation (Table 2).

According to the sonographic criteria 84 (87·5%) ulnar nerves were found to be enlarged in contrast to 67 (69·8%) nerves on clinical palpation. The cross sectional areas were significantly enlarged at all three levels in the patient group (Table 3), $P$ value for all $<0·001$.

### Table 1. Age and sex distribution of patients

| Age-range (In years) | Males | females | Total |
|----------------------|-------|---------|-------|
| < 10                 | 0     | 1       | 1 (2·08) |
| 11–20                | 8     | 3       | 11 (22·91) |
| 21–30                | 15    | 2       | 17 (35·41) |
| 31–40                | 8     | 1       | 9 (18·75) |
| 41–50                | 7     | 1       | 8 (16·66) |
| 51–60                | 1     | 0       | 1 (2·08) |
| 61–70                | 1     | 0       | 1 (2·08) |
| TOTAL                | 40    | 8       | 48 (100) |

### Table 2. Clinical Presentation

| Symptoms                  | No. of patients (%) |
|---------------------------|---------------------|
| Skin Lesions              | 38 (79·16)          |
| Pure Sensory Symptoms     | 14 (29·16)          |
| Pure Motor Symptoms       | 10 (20·83)          |
| Both Sensory and motor    | 14 (29·16)          |
| Neither sensory nor motor | 10 (20·83)          |
| Patients with Reaction    | 8 (16·6%)           |
Clinically 86 out of 96 ulnar nerves (89·6%) were abnormal having enlargement or neural deficit or both, 26 patients (52 nerves) had bilateral, and 15 had unilateral, enlargement of the ulnar nerve. The 67 enlarged nerves were divided into Grade 1 (46 nerves: 47·9%), Grade 2 (17 nerves: 17·8%) and Grade 3 (4 nerves: 4·2%).

The sonographic dimensions and frequency of morphologic alterations were higher with increasing clinical grade (Table 4). The difference between CSA of Grade 0 and Grade 2 was found to be statistically significant.

In our study, ulnar nerve thickening as evaluated by sonography showed a tendency to be more severe in the segment above the medial epicondyle. The maximum nerve enlargement is 4 cm above the medial epicondyle. ANOVA test was performed to evaluate the dimensions of each group of Ridley-Jopling classification and no significant difference was noted in these different groups, nor in the pure neuritic variety.

Of the 96 nerves examined in the leprosy patients, 66 out of 96 (68·8%) exhibited varying degrees of echotexture and vascular abnormalities and 30 (31·2%) of the nerves showed normal echo patterns.

The echotexture abnormalities seen were focal hypoechoic areas in 59 nerves (61.5%), loss of fascicular architecture in the same 59 nerves (61·5%) and focal hyperechoic areas in 47 nerves (49%).

Endo and perineural flow suggestive of increased neural vascularity by Colour Doppler imaging was observed in 16 and 30 of the 96 examined nerves, respectively. The presence of a nerve abscess was demonstrated in four nerves (4·2%), all above the medial epicondyle. Two patients showed the presence of thickening of cutaneous branches of ulnar nerve as well (Figure 10).

Five patients presented with Type 1 reaction and three with Type 2 reactions; 37·5% of nerves (six of 16) with clinical evidence of reaction showed endoneural vascularity as

### Table 3. Mean Sonographic measurements (CSA) of ulnar nerve at three levels in controls and leprosy patients

|                      | Above ME     | At Cubital Tunnel | Below ME    |
|----------------------|--------------|-------------------|-------------|
| Control Group        | 4·08 ± 0·14  | 4·55 ± 0·02       | 4·00 ± 0·13 |
| Patient Group        | 12·52 ± 1·67 | 8·94 ± 0·64       | 5·35 ± 0·26 |

CSA: Cross Sectional area, ME: Medial Epicondyle.

### Table 4. Number and percentage distribution of abnormal echotexture, Colour Doppler abnormality and CSA of various clinical grades

| Clinical Grade of Thickening | No of nerves | Abnormal echotexture (%) | Abnormal colour Doppler finding (%) | Mean CSA above ME as per sonography |
|------------------------------|--------------|--------------------------|------------------------------------|-----------------------------------|
| 0                            | 29           | 30·15%                   | 13/29 (44·82)                      | 6·24 ± 1·3                        |
| 1                            | 46           | 47·91%                   | 30/46 (65·21)                      | 12·46 (26·08)                     |
| 2                            | 17           | 17·77%                   | 13/17 (76·47)                      | 11/17 (64·7)                      |
| 3                            | 4            | 4·17%                    | 3/4 (75)                           | 3/4 (75)                          |
compared to 12.5% of nerves in patients without reaction (10 of 80). This difference was found to be significant ($P$ value $< 0.05$) using Fisher’s exact test.

**Discussion**

Our findings from HRUSG of the normal ulnar nerves in the control group are in accordance with previous studies done to ascertain normal echotexture of nerves. In the study by Jain *et al.* evaluation of the ulnar nerve in healthy subjects displayed no gender related difference in the mean CSA of the ulnar nerve.

The mean CSA of the ulnar nerve in our study in leprosy patients was 12.52 mm$^2$ against a normal of 4.08 mm$^2$ above the medial epicondyle. In our study, CSA values above the mean $\pm 2SD$ were considered abnormal. Ulnar nerve thickening was the main sonographic feature in the leprosy patients in our study and was present in 87.5% of nerves, which is in agreement with previously reported studies. In the study done by Elias *et al.* thickening on sonography of the ulnar nerve was reported in 90.5% of patients. They calculated the cut off for maximum cross sectional area using ROC curve and found it to be 9.8 mm$^2$. In one of the Asian studies done by Bathala *et al.* involving 100 healthy Indian subjects, the mean ulnar nerve CSAs were found to be $4.1 \pm 0.6$ mm$^2$ 3 cm distal to tip of the medial epicondyle; $4.7 \pm 0.6$ mm$^2$ at the tip of the medial epicondyle; and $4.4 \pm 0.6$ mm$^2$ 5 cm proximal to tip of the medial epicondyle.

In this study, we have specifically studied the correlation between clinical signs and sonographic findings and shown that in patients with known leprosy and no neurological signs or palpable nerves, enlarged dimensions can be identified in up to 90% of patients. Nerve thickening (87.5%) is the most common finding followed by echotexture abnormality (61.4%), and vascularity (31.2%).

There was no significant increase in dimensions in patients presenting with reactions ($P$ value $> 0.05$). This is in contrast to the study performed in 2009 by Jain *et al.* who concluded that nerves were enlarged especially in patients with Type 1 and Type 2 reactions. In our study, patients with reactions showed an increased frequency of endoneural vascularity, 37.5% as against 12.5% in nerves without reaction, and this difference was significant.

Martinoli *et al.* in their study of 58 nerves, concluded that the onset of active reversal reactions can be better indicated by endoneural colour flow signals as well as by an increased T2 signal and Gadolinium enhancement on MR studies. The overall sensitivity of Doppler US and MR to detect clinically recognised active reversal reaction phases was 74% and 92% respectively. The anti-reaction treatment is discontinued upon clinical amelioration but some patients develop repeated leprosy reactions even after a full course of treatment. This suggests a possible role of imaging to monitor the reactive process during therapy, especially when it is not clinically obvious whether a patient is in remission or not.

Besides enlargement, nerves in leprosy patients exhibited varying degrees of structural abnormalities. Four BT patients showed the presence of an abscess above the medial epicondyle. The region of abscess formation showed the presence of moving internal echoes within s/o liquefaction and abscess formation (Figure 7).

When patients were divided according to the Ridley-Jopling classification, there was no correlation with either the imaging groups or the nerve cross-sectional area, indicating that the clinical types of leprosy cannot be separated on the basis of USG. However, as in the majority of the leprosy population, most patients in our study had borderline forms of disease,
in which typical features of pauci- and multi-bacillary forms are often overlapping. The study by Martinoli et al. also did not reveal any differences in the nerve sizes of different leprosy groups.7

The immunological explanation for the diverse spectrum of clinical and histological appearances in leprosy, suggests that well-organised granulomas in tuberculoid skin lesions are also present within the cutaneous nerves and in larger nerve trunks. Two patients in our group showed thickening of the cutaneous branch of the ulnar nerve, which can be overlooked on clinical examination, as in our study, unless markedly enlarged (Figure 10).12

Clinical palpation is limited to the most superficial part of the nerve whereas sonography can be used to visualise a long segment of the nerve in one single image in a panoramic view and can evaluate the nerve in areas not accessible to palpation13 (Figures 8 and 9).
One important limitation of this study was that, for ethical and technical reasons, it was not possible to biopsy the ulnar nerve to confirm the neuropathy in our cases. The reference standard in the study was presence of nerve thickening detected clinically and neural symptoms in patients proven to have leprosy based on histopathologic, bacteriological or clinical criteria. Another important limitation was the lack of follow up to confirm amelioration of sonographic changes on treatment.

Although MRI provides precise imaging of nerves and higher sensitivity in detecting reversal reactions, its use in resource poor countries like India is limited. The high prevalence of leprosy demands a more accessible and affordable modality like ultrasound. The sonographic technique can detect nerve involvement by allowing measurement of ulnar nerve dimensions. Morphological assessment can also indicate leprosy neuropathy, while colour Doppler imaging can help in associated reactional states.
References

1. Jopling WH, McDougall AC. In: Handbook of Leprosy. 5th edition. New Delhi: CBS Publishers, 1996; pp. 1–10.
2. Agrawal A, Pandit L, Dalal M, Shetty JP. Neurological manifestations of Hansen’s disease and their management. Clin Neurol Neurosurg, 2005; 107: 445–454.
3. Weekly Epidemiological Record, 2013; 88: 365–380.
4. Khanna N. In: Illustrated Synopsis of Dermatology and Sexually Transmitted Diseases. First edition. Delhi: Peepee Publishers, 2005; pp. 198–209.
5. Croft RP, Nicholls PG, Steyerberg EW et al. A clinical prediction rule for nerve-function impairment in leprosy patients. Lancet, 2000; 355(9215): 1603–1606.
6. Schuring RP, Richardus JH, Sterber EW et al. Preventing nerve function impairment in leprosy: validation and updating of a prediction rule. PLoS Negl Trop Dis, 2008; 2: e28. Epub 2008 Aug 27.
7. Martinoli C, Derchi LE, Bertolotto M et al. US and MR imaging of peripheral nerves in leprosy. Skeletal Radiol, 2000; 29: 142–150.
8. Jain S, Visser LH, Praveen TL et al. High Resolution Sonography: A New Technique to Detect Nerve Damage in Leprosy. PLoS Negl Trop Dis, 2009; 3: e498.
9. Silvestri E, Martinoli C, Derchi LE et al. Echotexture of Peripheral Nerves: Correlation between US and Histologic Findings and Criteria to Differentiate Tendons. Radiology, 1995; 197: 291–296.
10. Elias J Jr, Nogueira-Barbosa MH, Feltrin LT et al. Role of ulnar nerve sonography in leprosy neuropathy with electrophysiologic correlation. J Ultrasound Med, 2009; 28: 1201–1209.
11. Bathala L, Kumar P, Kumar K, Visser LH. Ultrasonographic cross-sectional area normal values of the ulnar nerve along its course in the arm with electrophysiological correlations in 100 Asian subjects. Muscle & Nerve, 2013; 47: 673–676.
12. Lolge SJ, Morani AC, Chaubal NG, Khopkar US. Sonographically guided nerve biopsy. J Ultrasound Med, 2005; 24: 1427–1430.
13. Cooperberg PJ, Barberie JJ, Wong T, Fix C. Extended field-of-view ultrasound. Semin Ultrasound CT MRI, 2001; 22: 65–77.