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Original Article

Greater Auricular and Ulnar Nerve Damage in Leprosy: Clinical and Electrophysiological Comparison

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Clinically leprosy can have varied presentations ranging from an insignificant skin lesion to extensive disease causing profound disability and disfigurement by damaging peripheral nerves, eyes, bones and other tissues. Peripheral nerve involvement occurs sooner or later in the disease course leading to gross deformities and disabilities. Deformities in leprosy are secondary to nerve damage. However, by the time it clinically manifests, the nerve damage may already be quite advanced. If the preclinical damage is detected early, it can be prevented largely. The study was conducted in the Department of Dermatology, Venereology & Leprosy and Department of Neurology, Indira Gandhi Medical College, Shimla over a period of one year. This electrophysiological study included 20 patients with clinical manifestations of leprosy. 15/20 (75%) belonged to BL/LL types. 18 patients (90%) were multibacillary and 2(10%) were paucibacillary types. Nerve conduction velocity, amplitude and latency of greater auricular and ulnar sensory nerves were done. We found reduced conduction velocities, changes in latency and amplitude in the affected nerves. Ulnar nerve was more commonly involved than the greater auricular nerve. Out of 32 thickened ulnar nerves clinically, only 12 nerves (37.5%) had nerve function impairment. Two non-thickened nerves (2.5%) also had sensory impairment; in contrast 24 thickened nerves had normal functions. Thus, Nerve Conduction Studies can help in detection of early nerve impairment in some cases which otherwise may not be detected clinically. While overall these investigations appear to have limited value in diagnosis of disease and their prognostic value in monitoring the disease progression/response to intervention should be determined by follow-up studies. Valid conclusions with wider application value can only be drawn after carrying out follow up studies on a significant number of leprosy cases.

Keywords : Leprosy, Electrophysiology, Nerve Conduction, Neuropathy

Introduction

Leprosy is essentially a disease of the nerves, and most of the disabilities caused by leprosy are due to involvement of peripheral nerves. Peripheral nerve involvement may vary from involvement of an intradermal nerve in the cutaneous patches to a major lesion in the peripheral nerve trunk. Neuropathy is often clinically silent in its

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evolution making early diagnosis challenging. Clinical neurological examination, especially of sensory function, is essentially subjective in that it is based on a certain level of patient awareness.

Nerve conduction studies are the gold standard for detecting early changes in peripheral neuropathy (Khambati et al 2009). During the last over 40 years period several studies on nerve conduction in leprosy have been carried out (Antia et al 1975, Dhonde et al 1983, Gourie-Devi 1984, Ghiglione et al 2004, Soysal et al 2004, Hussain & Malaviya 2007, Khambati et al 2009, Chaurasia et al 2011, Vashisht et al 2014, Chhabra et al 2015), which have shown that electro-physiological studies may detect changes even in clinically normal nerves. However, greater auricular nerve has been studied to a limited extent with only Gourie-Devi (1984) studying it previously in the year 1984. As the spectrum of disease has been changing with impact of multi-drug campaigns, there is need to periodically assess the value of such investigations. Therefore, a prospective clinical study by means of clinical neurological examination and neuro-physiological studies was performed to compare the nerve function impairment of greater auricular and ulnar sensory nerves in leprosy patients.

Materials and Methods

The present study was conducted over a period of one year in the Department of Dermatology and Department of Neurology, Indira Gandhi Medical College, Shimla. Diagnosed (on treatment) cases of Hansen's disease fulfilling the WHO criteria and attending the Out Patient Department (OPD) were included in the study. However, cases with associated diabetes mellitus, cervical trauma, neurological disease, cardiovascular disease, patients with pace makers, chronic alcoholics, patients of age less than 6 years and cases during the reaction episodes were excluded from the study.

In each case, informed written consent, detailed history, clinical examination and slit skin smear examination was done. Sensory examination was carried out methodically in every patient with temperature, touch and pain being tested over the lesions, normal skin and extremities. Any deformities present were noted. We used a questionnaire, skin and electrophysiological examination for our study. Nerve conduction of greater auricular and ulnar sensory nerves was done using machine – 4 channel EMG system of Sigma Neurowork from Germany.

The general principle of nerve conduction study is that the recording electrode is placed over nerve segment to be studied. The reference electrode for sensory response is placed distal to and on the nerve segment being studied. The ground electrode is usually placed on the body prominence between the stimulating and recording electrodes (Suneetha & Rao 2010). This was followed in the present study.

The routine sensory conduction techniques for greater auricular and ulnar sensory nerves are:

Greater auricular study : Greater auricular nerve was studied by Becser's method (Oh 2003), the recording and stimulation sites were as under:

Recording site : Posterior lower auricle (ear lobe) with the reference electrode placed slightly above the middle posterior part approximately 2.5 cm cranial to the active electrode.

Stimulation site : Posterior border of sternocleidomastoid muscle, 6 to 7 cm from the external acoustic meatus.

Ulnar sensory study : Ulnar nerve was studied by the method of Preston & Shapiro (2005), the recording and stimulation sites were as under:

Recording Site : Little finger (digit 5) - Ring electrodes with G1 placed over the metacarpal-phalangeal joint, G2 placed 3-4 cm distally over the distal interphalangeal joint.

Stimulation Site : Wrist: medial wrist, adjacent to the flexor carpi ulnaris tendon.

The interpretation of electrophysiological functions of nerve trunks was based on the analysis of three basic criteria - velocity, latency and amplitude of the evoked response (Fig. 1). The various parameters studied in NCS were sensory nerve action potential (SNAP), onset latency and conduction velocity. The normal values for parameters studied were taken from the reference books by Oh (2003) and Preston & Shapiro (2005) (Table 1).

Results

Demographic profile : The study included 20 patients, 15 males and 5 females (male: female ratio of 3:1) with an age range of 17 to 50 years (32.5 ± 7.81 years). 90% of patients were in the age group 15 - 44 years (Fig. 2). 70% patients were from the state of Himachal Pradesh while 30% were immigrants. Out of the 6 immigrant patients, 5 (83.33%) were from Nepal and 1 (16.66%) was from other state. 14 (70%) patients had occupations involving strenuous physical activities (manual labour/farming).

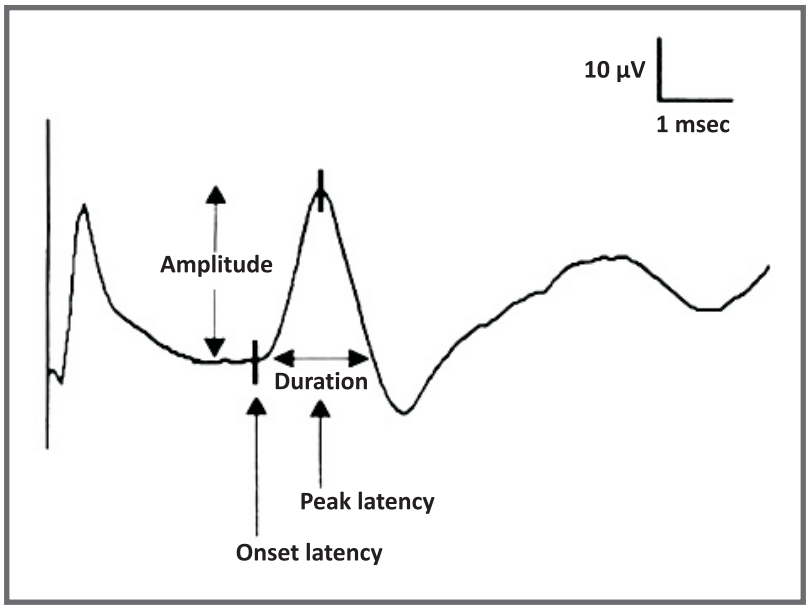

Fig 1 : Sensory nerve action potential (SNAP) investigated in the study

Table 1 : Normal values in Nerve conduction studies

Nerve	Record	Amplitude (µV)	Conduction Velocity(m/s)	Latency (ms)
Greater auricular	Posterior lower auricle	≥ 0.6	≥ 30.7	2
Ulnar Sensory	Digit 5	≥ 17	≥ 44	3.1

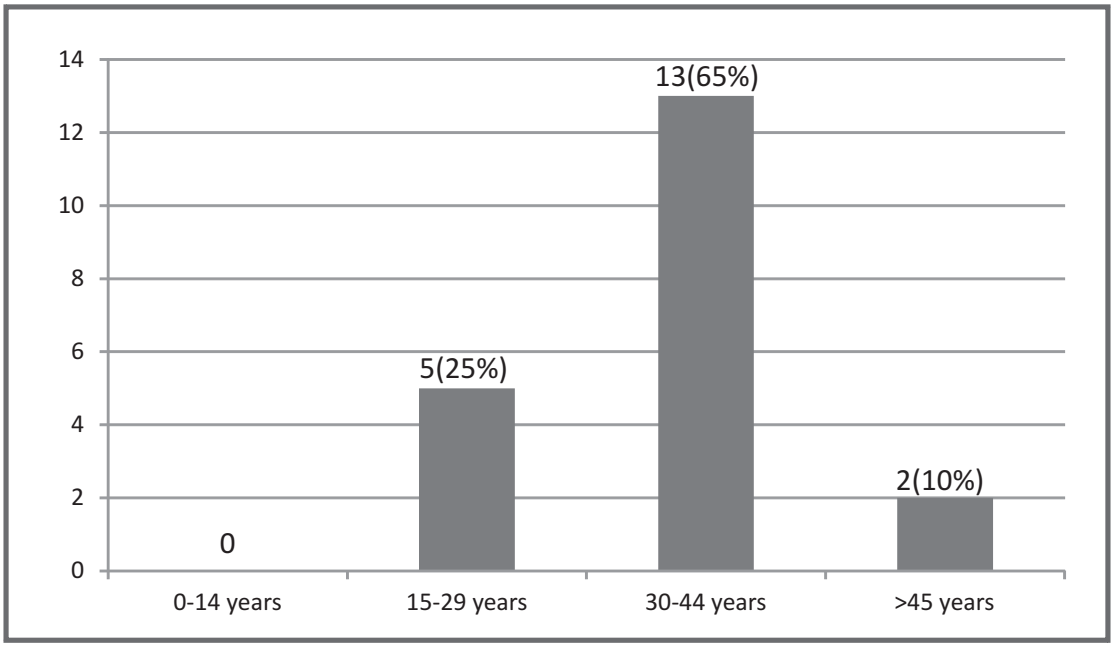

Fig 2 : Age distribution of cases included in the study.

Table 2 : Disease spectrum of leprosy cases included

n	TT	BT	BB	BL	LL	Pure neuritic	Indeterminate
20	0	5 (25%)	0	7 (35%)	8 (40%)	0	0

Clinical disease profile : History of contact was elicitable in 5 patients (25%). In all of these patients, the contact was within the household. 18 patients (90%) were multibacillary and 2 (10%) were paucibacillary. Skin smears were positive in 14 patients at diagnosis and they were treated as multibacillary cases. Smears were negative in 6 cases. Out of these, 4 were treated as multibacillary cases. However, 2 (10%) cases with a negative skin smear were treated as paucibacillary.

Disease spectrum : Most of the patients (75%) were in the lower spectrum of the disease (BL/LL) while 60% were in the borderline spectrum. At the time of diagnosis, 3 patients were seen downgrading from BT to BL and 1 from BL to LL (Table 2).

Disease manifestations : On clinical examination skin lesions were present in all 20 patients. Other manifestations of the disease are shown in Fig. 3.

Nerve thickening : Greater auricular nerve thickening was seen in 7 (35%) patients i.e. 13 nerves, with bilateral involvement in 6 patients and unilateral involvement in one patient. Ulnar nerve thickening was seen in 17 (85%) patients i.e. 32 nerves, with bilateral involvement in 15 patients and unilateral involvement in 2 patients.

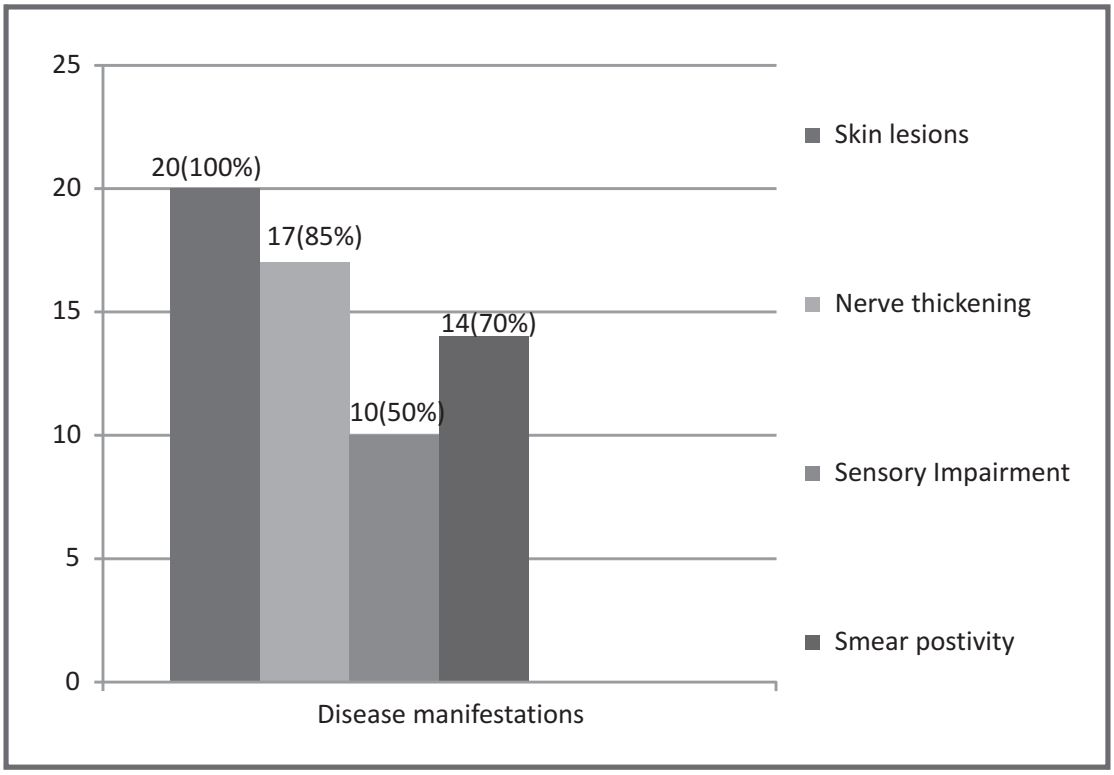

Fig 3 : Profile of disease in cases included in the study

Nerve function impairment : Nerve function impairment (greater auricular and ulnar sensory) on nerve conduction studies was found in 10 (50%) patients. The results of nerve conduction study are shown in Table 3.

All the patients with nerve function impairment were multibacillary type. Nerve function impairment was absent in paucibacillary patients. 8 (80%) patients with nerve impairment had occupations involving strenuous physical activities. Based on the spectrum, all the patients with nerve function impairment were of lower spectrum (BL/LL). It was found that the wulnar sensory nerves (30%) were though marginally more commonly involved than the greater auricular nerves (27.5%) (Table 4), this is not significant.

Nerve function impairment was present in 11 (27.5%) greater auricular nerves. Out of 13 thickened greater auricular nerves, 9 nerves (69.2%) had nerve function impairment while 4 thickened greater auricular nerves had normal nerve conduction studies. However, 2 nerves with nerve impairment had non thickened nerves.

Out of 32 thickened ulnar nerves clinically, only 12 nerves (37.5%) had nerve function impairment. All the patients with nerve impairment had thickened ulnar nerve.

Out of the total 23 nerves with nerve function impairment, mixed type (47.8%) was the most

Table 3 : Results of Nerve Conduction study

S. No.	Type of leprosy	Greater Auricular - Sensory						Ulnar - Sensory					
		Rt		Lt				Rt		Lt			
		Lat. (msec)	Ampl. (µV)	Lat. (msec)	Ampl. (µV)	Lat. Diff	Ampl. Diff	Lat. (msec)	Ampl. (µV)	Lat. (msec)	Ampl. (µV)	Lat. Diff	Ampl. Diff
1	BT	2.3	9.1	2.1	8	0.2	1.1	2.1	30.1	2.4	29.1	0.3	1
2	BT	2.2	7.5	2.5	7.9	0.3	0.4	2.2	21.4	2.9	22.4	0.7	1
3	BL	2.1	5.6	NS	NS	—	—	2.5	17.8	2.3	11.1	0.2	6.7
4	BL	1.9	11.8	1.9	9.8	0	2	2.4	28.7	2.6	29.6	0.2	0.9
5	BL	2.5	8.9	2.3	8.1	0.2	0.8	2.3	29.9	2.5	29	0.2	0.9
6	BT	1.3	15	1.8	17.1	0.5	2.1	1.9	23.5	2.1	27	0.2	3.5
7	LL	1.2	11.5	1.6	15.7	0.4	4.2	2	22.6	2.1	31	0.1	8.4
8	LL	2	4.3	NS	NS	—	—	NS	NS	NS	NS	—	—
9	BL	3.7	7.2	2.7	13.5	1	6.3	2.6	28.7	2.8	22	0.2	6.7
10	BT	1.8	15.8	1.8	12.4	0	3.4	2.2	40.1	2.1	28.1	0.1	12
11	LL	NS	NS	NS	NS	—	—	2.6	7.2	4	5.6	1.4	1.6
12	BL	3.5	8.9	2.2	12.3	1.3	3.4	3.4	25.2	2.2	34.6	1.2	9.4
13	LL	1.2	21.4	3	7.2	1.8	14.2	NS	NS	NS	NS	—	—
14	LL	1.9	15.6	2	1.4	0.1	14.2	2.3	24.1	2.5	18.2	0.2	5.9
15	BT	2	9.8	1.6	7.2	0.4	2.6	2	46.9	2.3	25	0.3	21.9
16	LL	0.7	46.9	1.9	15.4	1.2	31.5	3.1	20.6	3.3	18	0.2	2.6
17	BL	NS	NS	1.7	9.6	—	—	2.4	18.8	2.6	20.9	0.2	2.1
18	LL	0.8	5.6	1.2	10.8	0.4	5.2	2.4	32.6	3	13	0.6	19.6
19	BL	9.8	21.3	0.7	11.9	9.1	9.4	2.4	23.9	2.4	31.6	0	7.7
20	LL	NS	NS	NS	NS	—	—	NS	NS	4.4	17.1	—	—

(La. diff - latency difference; Ampl. diff - Amplitude difference between the two sides; NS - Not Stimulable)

Table 4 : Sensory nerve function impairment on NCS

NERVE	NERVES	PATIENTS
Greater auricular	11	8
Ulnar sensory	12	8
Total	23	10

Table 5 : Type of nerve function impairment

TYPE	VELOCITY	LATENCY	AMPLITUDE
Axonal	N/Slight ↓	N/Slight ↓	↓↓↓
Demyelinating	↓↓↓	↑↑↑	N/Slight ↓
Mixed	↓↓↓	↑↑↑	↓↓↓

common followed by demyelinating (30.4%) and axonal (21.7%) types.

Out of the 10(50%) patients with nerve function impairment, 1 patient (5%) had ulnar and greater auricular nerves of both sides involved while 4 patients (20%) had 3 nerves involved, remaining 5 patients had either one or two nerves involved. Clinically 3 patients (4 nerves i.e. 5%) had no sensory impairment but nerve conduction study detected impairment in these patients.

Two non thickened nerves (2.5%) also had sensory impairment on NCS. Contrary to this thickened nerves may also have normal functions as in our study (24 nerves i.e. 53.3%). Thus, Nerve Conduction Studies can help in detection of early nerve impairment which was otherwise not detected clinically, as in our study.

Discussion

Nerve conduction studies are helpful in assessment of degree of nerve dysfunction, the type of fibres involved and for detecting subclinical involvement in leprous neuropathy.

Leprosy affects both the sexes; however, males are affected more often as compared to females, generally in the proportion of 2:1 (Thangaraj 1983). The male to female ratio of 3:1 was noted in our study. More number of male cases could be attributed to their greater mobility and increased opportunity for contact. Males are also more active in reporting to health facility for seeking treatment. Additionally, 30% of our patients were migrant workers, which predominantly consist of male population; also, in our state females cover most of their body parts which could lead to decreased detection of skin lesions. These could be the factors responsible for higher proportion of males in our study.

Another study from our state by Jindal et al (2009) also reported male to female ratio of 3:1, which was similar to our study. Chhabra et al (2015) also reported higher male to female ratio (2.3:1). 54.3% of patients were migrant workers in their study. The explanation given by them for the higher male to female ratio was similar to our study.

Leprosy can occur at any age but is more common in the age group of 20 - 30 years. Our study included 20 patients with the mean age of 32.5 ±

7.81 years. 90% of the patients were in the age group 15 - 44 years; all the patients in our study were above the age of 14 years. The percentage of childhood leprosy is low in our study which indicates absence of active transmission of the disease in the community. In our study 75% of the patients were in the middle age group (20-40 years) which is in accordance with the literature. In Jindal et al (2009) study, majority of patients (47.8%) was in the middle age grouping (20-40 years). In Chhabra et al (2015) study, the mean age of patients was 32.08 ± 15.46 years, which was similar to our study.

A large number of migrant labourers, especially from Nepal, travel to Himachal Pradesh for employment. Himachal Pradesh, a low endemic area for leprosy, is too getting its share of migrant leprosy as is evident from the data from our study. In our study 70%, patients were from the state of Himachal Pradesh while 30% were immigrants. In Jindal et al (2009) study also, 71.78% patients were from Himachal Pradesh while 28.22% patients were immigrants. 70% of our patients had occupations involving strenuous physical activities (manual labour/ farming). 30% patients had occupations involving light physical activity. Alam et al (1998) study also reported that a large majority of patients (78%) were involved in heavy manual work as farmers and labourers.

In our study, 25% gave a history of contact with a leprosy patient. In all of these patients, the contact was within the household. Rate of household contact in our series was higher than that reported by Jindal et al (2009), 9.2% as the ratio of MB cases is significantly higher in our study (90%) compared to Jindal et al (81.59%). It has been shown that the probability of finding familial occurrence of leprosy is higher in families that include a lepromatous patient; than in those where it does not (Kapoor 1963). Most of the other studies from India have included neighbourhood contacts also hence the data could not be compared. Van Beers et al (1999) have shown that risk of a person developing leprosy is four times higher when there is a neighbourhood contact and up to nine times higher when the contact is intra-familial.

90% of our patients were multibacillary and rest 10% were paucibacillary. In Jindal et al (2009) study also the majority of the patients were multibacillary (81.59%) and 18.41% were paucibacillary. Skin smears were positive in 14 (70%) patients at diagnosis and they were treated as multibacillary cases. Smears were negative in 6 cases. Out of these, 4 were treated as multibacillary cases. However, 2 cases with a negative skin smear were treated as paucibacillary. 46% patients were smear positive in Jindal et al (2009) study, which is less than in our study as most of the patients (75%) were in the lower spectrum of the disease.

In the study of Murthy et al (2015), of the 100 patients, 55 were BT followed by LL (29), BL (8), TT (5), BB (2) and only one patient of indeterminate leprosy. Skin smear examination showed the presence of bacilli in 32% (4 cases of BL and 28 cases of LL).

In the clinical disease spectrum of our study, most of the patients (75%) were in the lower spectrum of the disease (BL/LL) while 60% were in the borderline spectrum.

In the study of Jindal et al (2009) , 53.98% patients were in the borderline spectrum followed by LL (33.12%) and polar tuberculoid leprosy (5.52%). Pure neuritic and indeterminate leprosy accounted for 3.06% each. The type of leprosy commonly present was LL followed by BT. This is in contrast to other studies which show BT, followed by TT to be commonest spectrum (Mahajan et al 2003, Singh et al 2009). The reason given by Jindal et al (2009) was that the Himachal Pradesh holds

a better position as compared to overall trend in India except for invisible deformity and MB cases, the ratio of which is significantly higher in Himachal Pradesh; another reason given was large load of immigrant population.

In our study also LL spectrum was the most common type as in Jindal et al (2009) study for the same reasons. However, the second most common spectrum in our study was BL in contrast to Jindal et al. which show BT as the second most common spectrum. This difference may be due to difference in proportion of multibacillary (81.59%) and paucibacillary (18.41%) compared to our study in which 90% patients were multibacillary type and rest 10% of patients were paucibacillary.

On clinical examination, skin lesions were found in all the patients of our study. Jindal et al *(2009)* reported skin lesions in 96.9% of the patients as 3.1% of the patients were of pure neuritic leprosy, compared to our study in which no patient had pure neuritic leprosy.

In our study 85% patients had one or more nerve thickening. Ulnar nerve thickening was seen in all 85% of these patients while greater auricular nerve thickening was seen in 35% of these patients. In a study by Chaurasia et al *(2011),* nerve thickening (one or more) was seen in 87.5% while ulnar nerve thickening was seen in 65% cases. This difference may be due to difference in proportion of multibacillary (52.5%) and paucibacillary (47.5%) compared to our study in which 90% patients were multibacillary type and rest 10% of patients were paucibacillary. In another study by Soysal et al *(2004),* 94.74% of patients had thickened nerves. Hussain and Malaviya (2007) detected ulnar nerve thickening in 70.8% cases while Vashisht et al (2014) observed ulnar nerve thickening in 72% patients. In a study by Gourie Devi (1984), greater auricular nerve thickening was seen in 41.67%. The variation in different studies may be due to different proportion of multibacillary and paucibacillary cases. This can be due to higher MB cases in Himachal Pradesh. A large number of places in Himachal Pradesh are far off and difficult to reach and people seek medical care only late in the disease process (Jindal et al *2009).*

In our study, nerve function impairment (NFI) on nerve conduction studies was found in 50% patients. All the patients with nerve function impairment were multibacillary type. Based on the spectrum, all patients with nerve function impairment were of lower spectrum (BL/LL). 80% patients with nerve impairment were involved in strenuous physical activities. Chaurasia et al *(2011)* also reported that the patients with multibacillary leprosy had significantly more severe changes on NCS as compared to paucibacillary leprosy. In contrast to our study, Hussain and Malaviya (2007) reported that the changes in multibacillary cases were less marked compared to paucibacillary. No explanation for the above finding was given in the above two studies.

In our study the patients with MB leprosy had significantly more severe changes on NCS as compared to PB leprosy since the number of patients of PB were also less (only 10%). Due to the study of only greater auricular/ulnar nerve and different spectrum of the disease in various studies, the results cannot be compared.

Nerve function impairment was present in 27.5% greater auricular nerves in our study. Out of 13 thickened greater auricular nerves, 9 nerves (69.2%) had nerve function impairment; however, 2 nerves with nerve impairment had non thickened nerves, 4 thickened greater auricular nerves had normal nerve conduction studies. Gourie Devi (1984) performed sensory nerve conduction study on 24 greater auricular nerves (12 patients); NFI was detected in 66.67%

nerves. All the eight thickened nerves and 8 of 16 clinically normal nerves in leprosy patients were found to have electrophysiological abnormalities. Greater auricular nerve thickening is considered as an important sign in the diagnosis of leprosy. However, in some normal individuals the nerve is easily palpable and may be thickened (Jopling & McDougall 1996).

On the other hand, patients with thickened ulnar nerves (on palpation), only 37.5% patients had nerve function impairment on NCS but all the patients with nerve impairment had thickened ulnar nerves. Vashist et al *(2014)* reported sensory deficit in the distribution of thickened ulnar nerve in 86% of thickened nerves. The lower percentage in our study may be attributed to uneven involvement of nerve fascicles or may be related to the chronological occurrence of nerve damage among different nerve fibres or fascicles in the same nerve, this point needs further studies on different grades of nerve damage in a sufficient number of leprosy patients before any conclusion can be made.

In our study, it was found that the ulnar sensory nerves (30%) were more commonly involved than the greater auricular nerves (27.5%), which is in conformity with the literature. Based on the changes in velocity, amplitude, and latency of the evoked response, the nerve function impairment is divided into three types – axonal, demyelinating and mixed type. Mixed type had changes of both axonal and demyelinating types (Table 5). In our study mixed (47.8%) was the most common type followed by demyelinating (30.4%) and axonal (21.7%) type which is consistent with the previous studies. Chaurasia et al *(2011)* also detected mixed type as the commonest type of nerve function impairment. In contrast Soysal et al *(2004)* reported predominantly axonal neuropathy, 68.42% of the patients had axonal neuropathy; while demyelinating and mixed neuropathies were seen in 15.79% of subjects each. Predominance of axonal type in their study could be due to higher percentage of patients with lower spectrum since the nerve damage in this spectrum is due to fibrosis of the nerves which results in axonal type of damage.

In our study, 5% nerves (15% patients) had no sensory impairment clinically but nerve conduction studies detected impairment. Thus, nerve conduction studies can help in detection of early nerve impairment which was not detected clinically, as in our study it was detected in 15% patients. 2.5% non thickened nerves also had sensory impairment on NCS. Contrary to this, thickened nerves may also have normal functions as in our study (24 nerves i.e.53.3%). Ghiglione et al (2004) detected nerve function impairment in 43.6% of clinically asymptomatic nerves whereas in our study it was 5%. This difference was due to more number of nerves studied in this study compared to our study. Hussain and Malaviya (2007) observed that even though clinically normal, 16% ulnar and 20% median nerves were electrically abnormal in leprosy. They also observed that it is difficult to decide whether or not a clinically enlarged nerve in a patient is necessarily at risk. If the nerve is enlarged but has normal electrophysiological functions, a further period of observation is indicated. Several workers (Antia et al 1975, Antia et al 1970, Donde et al 1983) have noted that normal sensory-motor conduction velocities could be found in the diseased nerves which could be explained by involvement of certain fascicles of the affected nerve with little or insignificant involvement of others. Chaurasia et al (2011) also detected NFI before it was clinically evident. Vashisht et al *(2014)* also found changes in NCS in the affected nerves.

From this study, it can be concluded that the nerve conduction studies can reveal leprous

neuropathy before it becomes clinically evident, therefore neuro-physiological examination may be done along with the clinical examination at the time of diagnosis where ever facilities are available. Although normal individuals with well developed neck muscles can have thickened greater auricular nerves; the nerve conduction studies can further help in earlier diagnosis in countries where leprosy is widely prevalent and where such facilities are present. Such investigations may also help in monitoring the response to therapy and in determining the prognostic value of nerve deficit detected by electrophysiological investigations. This will enable us to prevent and manage disabilities and improve the quality of life of the patients. It would be appropriate to assess these benefits in properly conducted prospective studies.

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