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Original Article

Nerve Damage in Leprosy: A Comparison of clinical and electrophysiological Study of ulnar and Median Nerves

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Abstract
Background: *Peripheral nerve trunk involvement in leprosy is very common. However, by the time it becomes clinically apparent, the damage is quite advanced. If the preclinical nerve damage is detected early, the deformities and disabilities can be prevented to a large extent.*
Materials and Methods: *We conducted an electrophysiological study on 40 patients with clinical manifestions of leprosy. This study was done to assess the nerve conduction velocity, amplitude and latency of ulnar and median nerves.*
Results and Conclusion: *We found reduced conduction velocities, besides changes in latency and amplitude in the affected nerves. Changes in sensory nerve conduction were more pronounced. Ulnar nerve was more commonly involved than the median nerve.*
Keywords: *Leprosy, electrophysiology, nerve conduction, neuropathy.*

Introduction

Leprosy neuropathy is complex, with the superposition of acute and chronic sensory, motor and/or autonomic events. A stage of functional blockade of conduction of nerve impulse almost always precedes visible pathological changes in the nerve.[1]

The role of electrophysiological evaluation of nerve function in the diagnosis and assessment of different neuropathies is well established. There have been few studies of nerve conduction in leprosy and these studies have shown that marked slowing of conduction may occur in leprosy affected nerves. A significant decline of motor nerve conduction velocities has also been reported in clinically normal nerves in leprosy.[1]

Nerve conduction studies (NCS) are the gold standard for detecting peripheral neuropathy.[2]

Therefore a prospective clinical study by means of clinical neurological examination and neurophysiological studies was performed to compare the nerve function impairment of ulnar and median nerves in leprosy patients.

Material and Methods

The present study was conducted over a period of one year. Diagnosed (on treatment) cases of Hansen's disease who fulfilled the WHO criteria and attending the Out Patient Department 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, cases with grade 2 deformity upper limbs and cases during the reaction episodes were excluded from the study.

In each case, informed written consent, detailed history and thorough examination with reference to clinical involvement in leprosy was done. In all cases slit skin smear examination was done. Sensory examination and voluntary motor testing was performed. Any deformities present were noted. We used a questionnaire, skin and electrophysiological examination for our study. Nerve conduction of ulnar and median (motor and sensory) nerves was doneusing machine – 4 channel EMG system of Sigma Neuro work from Germany.

The general principle of nerve conduction study is that the percutaneous stimulation for nerve conduction is performed with surface electrodes placed at appropriate anatomic locations along the course of nerve segment being studied. The interpretation of electrophysiological functions of nerve trunks is usually based on the analysis of three basic criteria - velocity, latency and amplitude of the evoked response.[3]The various parameters studied in NCS were distal motor latency, compound muscle action potential and conduction velocity for motor nerves. However in case of sensory nerves, sensory nerve action potential (SNAP), onset latency and conduction velocity was recorded (Table-1[4]).

Results

Demographic Profile

The study included 40 patients, 30 males and 10 females (male:female ratio of 3:1) with an age range of 10 to 52 years (32.9 +10.14years).85% of patients were in the age group 15 - 44 years. The rest of the age wise distribution of patients is shown in Figure 1.

57.5% patients were from the state of Himachal Pradesh while 42.5% were immigrants. Of the17 immigrant patients, 13(76%) were from Nepal and 4 (24%) were from other states. 20(50%) patients had occupations involving strenuous physical activities (manual labour/farming).

Clinical Disease Profile

History of contact was elicitable in14 patients (35%).In all of these patients, the contact was within the household. 33(82.5%) patients were multibacillary and 7(17.5%) were paucibacillary. Skin smears were positive in 20 patients at diagnosis and they were treated as multibacillary cases. Smears were negative in 20 cases. Out of these, 13 were treated as multibacillary cases. However, 7(17.5%) cases with a negative skin smear were treated as paucibacillary.

Disease Spectrum

Most of the patients (72.5%) were in the borderline spectrum.60% were in the lower spectrum of the disease (BL/LL).At the time of diagnosis, 7 patients were seen downgrading from BT to BL, 2 from BL to LL and 1 from TT to BT(Table -2).

Disease Manifestations

On clinical examination skin lesions were present in all 40 patients. Other manifestations of the disease are shown in Figure-2.

Nerve thickening

Ulnar nerve thickening was seen in 32(80%) patients, 26 patients had thickened ulnar nerve of both sides while 6 patients had thickened ulnar

nerve of only one side. Median nerve was not thickened in any patient.

Nerve function impairment

Nerve function impairment (ulnar and median) on nerve conduction studies was found in 14(35%) patients. All the patients with nerve function impairment were multibacillary type. Nerve function impairment was absent in paucibacillary patients. 8(57.14%) patients with nerve impairment were manual labourers. Based on the spectrum72% of patients with nerve function impairment were of lower spectrum (BL/LL) (Figure-3).

Of 32 patients (58 nerves) with thickened ulnar nerves clinically, only 11patients (17 nerves-29%) had nerve function impairment.. All the patients with nerve impairment had thickened ulnar nerve. It was found that the ulnar nerves (21.25%) were more commonly involved than the median nerves (13.75%), while sensory nerves (16.9%) were more commonly involved than the motor nerves (8.75%). Ulnar sensory (21.25%) was more severely involved than the median sensory (12.5%) but median motor (11.25%) was involved more than the ulnar motor (6.25%) (Table-3).

Out of 28 nerves with nerve function impairment, axonal type (50%) was the most common followed by demyelinating (25%) and mixed (25%) type in equal proportion.

3 patients (7.5%) had ulnar and median nerves of both sides involved while 2patients (5%) had both ulnar and median nerve involvement of one side only. 1 patient (2.5%) had median motor involvement without sensory involvement.

6patients (15%) had only sensory impairment clinically but on nerve conduction studies, both sensory and motor impairment was found in these patients. 1patient (2.5%) had no sensory impairment clinically but nerve conduction study detected sensory impairment. Thus, Nerve Conduction Studies can help in detection of early nerve impairment which was otherwise not detected clinically, as in our study it was detected in 7 patients (17.5%).

Table- 1: Nerve conduction studies normal values [4]

Nerve	Record	Amplitude (μV)	Conduction Velocity(m/s)	Latency (ms)
Median Motor	**APB**	**≥4.0**	**≥48**	**≤4.2**
Ulnar Motor	**ADM**	**≥3.7**	**≥49**	**≤ 3.4**
Median Sensory	**Digit 2**	**≥17**	**≥44**	**≤3.5**
Ulnar Sensory	**Digit 5**	**≥17**	**≥44**	**≤3.1**

APB: Abductor Pollicis Brevis
ADM: Abductor Digiti Minimi

Table 2: Disease spectrum

n	TT	BT	BB	BL	LL	Pure neuritic	Indeterminate
40	**2(5%)**	**14(35%)**	**0**	**15(37%)**	**9(23%)**	**0**	**0**

Table-3: Sensory/motor nerve function impairment

NERVE	NERVES	PATIENTS
ULNAR SENSORY	**17**	**11**
ULNAR MOTOR	**5**	**4**
MEDIAN SENSORY	**10**	**8**
MEDIAN MOTOR	**9**	**6**

Table-4: Type of Nerve Function Impairment

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

Figure-1: Age distribution

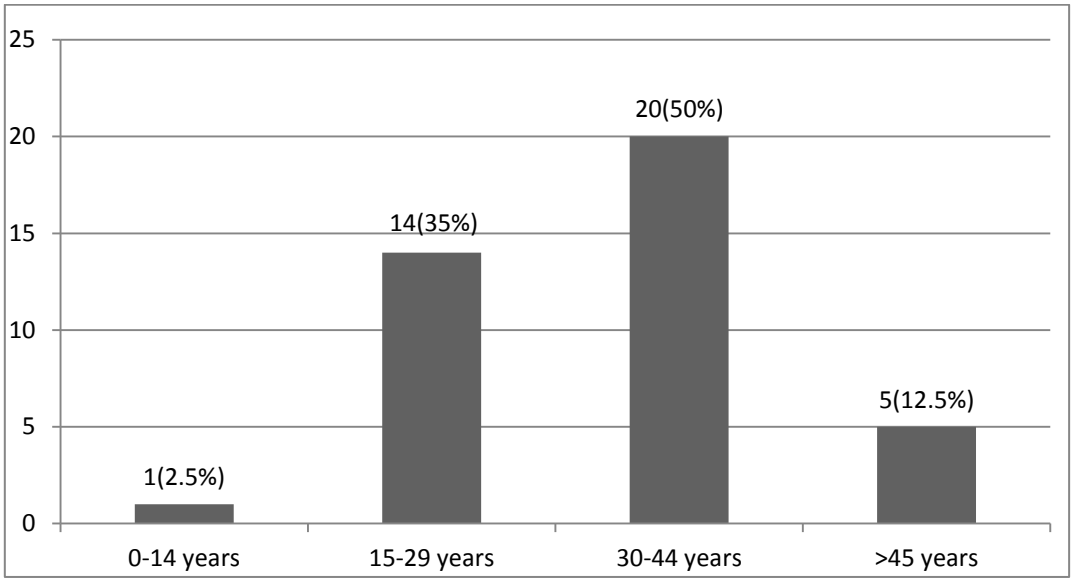


Figure-2: Disease manifestations

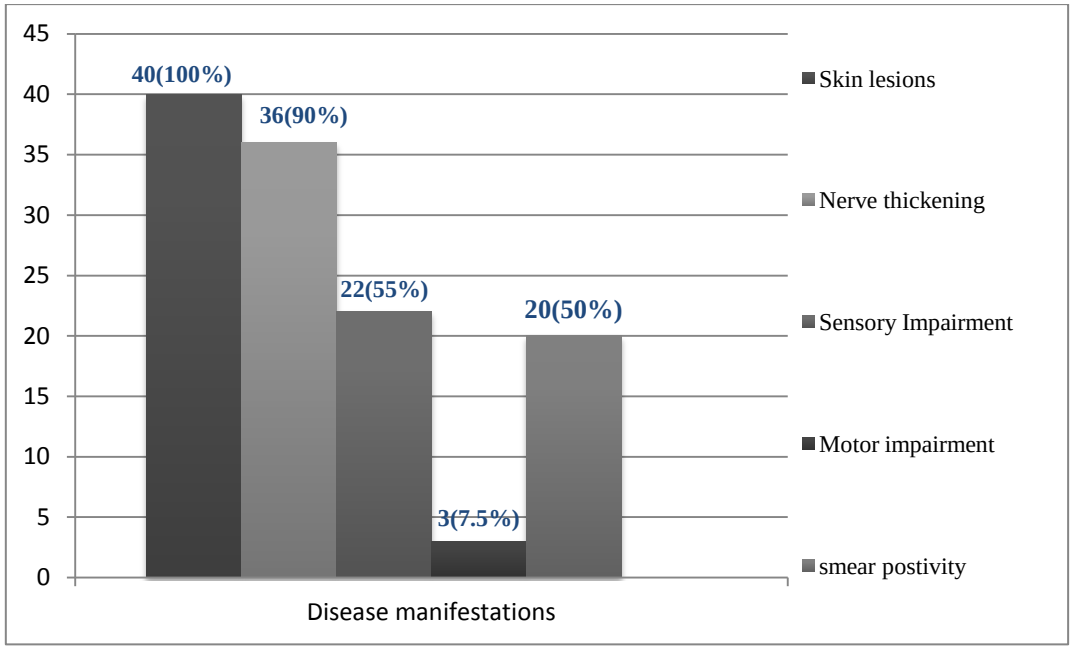
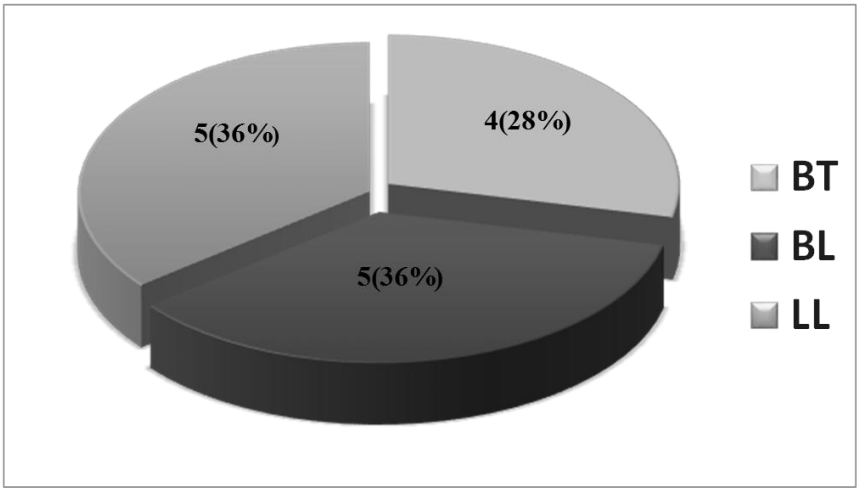


Figure- 3: Nerve function impairment based on the spectrum of the disease



Discussion

Leprosy is one of the principal causes of non-traumatic neuropathy. Leprosy affects both the sexes; however, males are affected more often as compared to females, generally in the proportion of 2:1.[5] 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, 42.5% 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.

In another study from our state by Jindal *et al.*[6] also reported male to female ratio of 3:1, similar to our study. Chhabra *et al.*[7] 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 40 patients with the mean age of 32.9 +10.14 years. 85% of patients were in the age group 15 - 44 years, 2.5% in the age group of less than 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 65% of patients were in the middle age group (21-40 years) which is in accordance with the literature. In Jindal *et al.*[6] study majority of patients (47.8%) were in the middle age group (20-40 years) and 13.49% patients were less than 20years of age. In Chhabra *et al.*[7]study the mean age of patients was 32.08 ±15.46 years which was similar to our study.

A large number of migrant labour especially from Nepal, Bihar and Uttar Pradesh, travel to Himachal Pradesh for employment. Himachal Pradesh, a low endemic area for leprosy, is too getting itsshare of migrant leprosy as is evident from the data from our study. In our study 57.5% patients were from the state of Himachal Pradesh while 42.5% were immigrants. Of 42.5% immigrant patients, 32.5% patients were from Nepal and 10% patients were from outside states. In Jindal *et al.*[6] study 71.78% patients were from Himachal Pradesh, 28.22% patients were immigrants. The higher percentage of indigenous cases from Himachal Pradesh in Jindal *et al.*[6]study compared to our study could be an indicator of improved leprosy scenario in the state.

50% of our patients had occupations involving strenuous physical activities (manual labour/ farming). 32.5% patients had occupations involving light physical activity. Alam *et al.*[8] reported that a large majority of patients (78%) were involved in heavy manual work as farmers and labourers. Lower percentage of patients involved in heavy work in our study could be due to exclusion of patients with type II deformity upper limbs since the patients involved in heavy work also have more chances of having higher grades of deformities.

In our study 35% gave a history of contact with aleprosy 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.*[6] (9.2%). Most of the other studies from India have included neighbourhood contacts also and therefore the data could not be compared. Van Beers *et al.*[9]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.

82.5% of our patients were multi bacillary and rest 17.5% were paucibacillary. In Jindal *et al.*[6]study also the majority of the patients were multibacillary 81.59% and 18.41% were paucibacillary as in our study.

Skin smears were positive in 20(50%) patients at diagnosis and they were treated as multibacillary cases. Smears were negative in 20cases. Out of these, 13 were treated as multibacillary cases. However, 7cases with a negative skin smear were

treated as paucibacillary. Of 24patients of lower spectrum (BL/LL) 20 patients were smear positive, those 4 with smear negativity had downgraded from BT to BL.46% were smear positive in Jindal *et al.*[6] study which is more than in our study which may be due to exclusion of patients with grade II deformity upper limbs in our study excluding large number of patients oflower spectrum.

In Murthy *et al.*[10]study of 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 only for 4 cases of BL (50% as in our study) and 28cases of LL. Out of the eight cases diagnosed as BL, 3 cases showed features of BT. On tissue section, they were negative for AFB. Possibly they were clinically also BT but because of numerous lesions and bilateral distribution they were diagnosed as BL. One case was LL histologically and this is understandable. Many a time, the clinical diagnoses do not match the histological features.

In the clinical disease spectrum of our study, most of the patients, i.e 72.5%5 were in the borderline spectrum. Most common being the BL (37.5%) spectrum followed by BT (35%).60% were in the lower spectrum of the disease (BL/LL).

In Jindal *et al.*[6] study 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).[11,12] The reason given by Jindal *et al.* 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 by immigrantpopulation.[6]

In our study BL spectrum was the most common type compared to LL spectrum in Jindal *et al*, as we had excluded the patients with type II deformity upper limbs thus excluding most of the patients of LL spectrum.

On clinical examination skin lesions were present in all the patients in our study. Jindal *et al.*[6] 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 90% patients had one or more nerve thickening. Ulna nerve thickening was seen in 80% patients. In a study by Chaurasia *et al.*[13]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 which82.5% patients were multibacillary type and rest 17.5% of patients were paucibacillary. In another study by Soysal *et al.*[14]94.74% of patients had thickened nerves which was almost similar to our study. Sajid and Malaviya[15] detected ulnar nerve thickening in 70.8%cases while Vashisht *et al.*[16] observed ulnar nerve thickening in 72% patients. The variation in different studies may be due to difference indifferent 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.[6]

In our study nerve function impairment on nerve conduction studies was found in 35% patients. All the patients with nerve function impairment were multi bacillary type. 72% of patients with nerve function impairment on NCS were of lower spectrum (BL/LL). 50% patients with nerve impairment were manual labourers. Chaurasia *et al.*[13] also reported that the patients with multi bacillary leprosy had significantly more severe changes on NCS as compared to paucibacillary leprosy. In contrast to our study Sajid and Malaviya[15] 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 17.5%), and also the patients with grade II deformity upper limbs had been excluded, thus excluding the majority of patients in whom the nerve function impairment could have been detected. Due to the exclusion criteria adopted, study of only ulnar/ medial nerve, spectrum of the disease are thus different, which cannot be compared.

Patients with thickened ulnar nerves on palpation, only 29% patients had nerve function impairment on NCS but all the patients with nerve impairment had thickened ulnar nerves. Vashist *et al.*[16] reported sensory deficit in the distribution of thickened ulnar nerve in 86% of thickened nerves. The lower percentage in our study is due to exclusion of patients with type II deformity of upper limbs.

In our study it was found that the ulnar nerves (21.25%) were more commonly involved than the median nerves (13.75%), while sensory nerves (16.9%) were more commonly involved than the motor (8.75%), which is in conformity with the literature. Ulnar sensory (21.25%) was more severely involved than the median sensory (12.5%) but median motor (11.25%) was involved more than the ulnar motor(6.25%).Ramadan *et al.*[17] also detected involvement of median motor more than the ulnar motor, motor nerve conduction of median nerve was abnormal in 72.5%, while motor nerve conduction of ulnar nerve was abnormal in 70% and sensory nerve conduction of ulnar nerve was abnormal in 77.5% of the total. The involvement of median motor more than ulnar motor in our study and Ramadan *et al.* 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 anyconclusion can be made.

Sajid and Malaviya[15]and Vashisht *et al.*[16]also found changes in NCS in the affected nerves. Changes in sensory nerve conduction were more pronounced than motor which is in accordance with the literature.

In our study only 1 patient had median motor impairment without sensory impairment on NCS. In another study by Gupta *et al.*[18] motor nerve conduction velocity was found to be reduced in more number of patients when compared with sensory nerve. The sensory fibres are damaged early in leprosy and therefore show more quanta of changes in conduction velocities as compared to motor nerve fibres in the early stages of damage.[15] However, the amplitude changes are much more marked for motor nerve fibres[19] which may explain the median motor impairment without sensory impairment in oneof our patients.

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 has changes of both axonal and demyelinating types (Table-4).In our study axonal type (50%) of nerve function impairment wasthe most common followed by demyelinating (25%) and mixed (25%) type in equal proportion. In contrast to previous studies predominance of axonal type in our study could be due to higher percentage (60%) of patients with lower spectrum (BL/LL) since the nerve damage in this spectrum is due to fibrosis of the nerves which results in axonal type of damage. Soysal *et al.*[14] also 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. In contrast to our study and consistent with the previous studies Chaurasia *et al.*[13]detected mixed (axonal as well as demyelination) type as the commonest type of nerve function impairment.

In our study 15% patients had only sensory impairment clinically, but were found to have both sensory and motor impairment on NCS. 1(2.5%)

patient had no sensory impairment clinically but nerve conduction studies detected sensory 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 17.5% patients. Ghiglione *et al.*[20] detected nerve function impairment (NFI) in 43.6% in clinically asymptomatic nerves (C.f. our study 17.5). This difference was due to more number of nerves studied in this study compared to our study. Sajid and Malaviya[15]observed that even though clinically normal, 16% among ulnar and 20% among median nerves were electrically abnormal in leprosy, mean 18% in this study is almost equal to our study. Chaurasia *et al.*[13] also detected NFI before it was clinically evident.

Conclusion

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 should be done along with the clinical examination at the time of diagnosis where available.

All the cases with nerve function impairment needs regular follow up to identify the patients with progressing nerve involvement. It is important to counsel the patients to report early in case of reactions and new impairments. This will enable us to prevent and manage disabilities and improve the quality of life of the patients.

NCS is safe, rapid and non-invasive technique making it a useful investigation where available

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