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Original Article

Dermatology Section

A Cross-sectional Study on the Electrophysiological Profile of Leprosy Patients in a Tertiary Care Institute in Chhattisgarh, India

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ABSTRACT

Introduction: Leprosy is a bacterial infection caused by *Mycobacterium leprae*. It mainly infects skin, mucosa and nerves. Neural involvement is primarily due to the selective affinity of Schwann cells for lepra bacilli. Nerve involvement leads to Nerve Function Impairment (NFI) which presents as sensory and/or motor deficit, cutaneous nerve thickness or painful neuritis eventually lead to deformity and disability. NFI can be accessed by Nerve Conduction Study (NCS). Early diagnosis and treatment plays important role in the prevention of permanent nerve damage due to leprosy.

Aim: To study the electrophysiological profile of Pure Neuritic Leprosy (PNL), Tuberculoid Hansen's Disease (TTHD) and Borderline Tuberculoid Hansen's Disease (BTHD).

Materials and Methods: A cross-sectional study was conducted on 63 newly diagnosed patients in dermatology Out Patient Department (OPD) in Late Shri Lakhiram Agrawal Memorial Medical College, Raigarh, Chhattisgarh, India, from June 2020 to May 2021. The NCS was conducted after obtaining approval from the Institutional Ethical Committee. The bilateral ulnar nerve, median nerve, common peroneal nerve, posterior tibial nerve and sural nerve were assessed by NCS for each patient. Data was collected and analysed by unpaired student's t-test using Statistical Package for the Social Sciences (SPSS) software version 21.0.

Results: Total 378 nerves were examined for nerve thickness. Total 106 nerves were found to be thickened. The most common neuropathy found was of demyelinating sensory and sensorimotor type seen in 21 (33.33%) patients. A total of 12 (19.05%) patients had both axonal and demyelinating neuropathy (mix neuropathy). Only 5 (7.94%) patients had pure axonal neuropathy of sensorimotor or sensory nerves.

Conclusion: Most common neuropathy found was demyelinating sensory and sensorimotor neuropathy. The ulnar nerve was found to be the most common nerve involved in leprosy.

Keywords: Axonal neuropathy, Demyelinating neuropathy, Hansen disease, Nerve conduction study, Nerve function impairment

INTRODUCTION

Leprosy is a bacterial infection caused by *Mycobacterium leprae* which mainly affects the peripheral nervous system and skin. *Mycobacterium leprae* has affinity for temperature less than 37°C for its optimal growth, so it mainly involves skin, nasal mucosa and peripheral nerves where the temperature is lower than core body temperature [1]. *Mycobacterium leprae* is the only bacteria that affect nerves and Schwann cells. Leprosy patients often present with some level of NFI. Inspite of adequate treatment, some of the patients develop neuropathy during or after treatment. There can be as much as 30% damage in nerve fibre without any clinical manifestation [2]. The main site of nerve involvement is terminal nerve fibres in skin lesions and nerve trunks where they are superficially located (colder), in the fibro-osseous grooves (easily compressed), in trauma prone sites (repeated trauma) and when a skin lesion is overlying the nerve trunk [3]. The presentation of nerve lesions ranges from silent neuropathy to severe neuritis. Leprosy is classified by different classification systems. Ridley-Jopling classification leprosy is divided into five groups: TT: Tuberculoid leprosy, BT: Borderline tuberculoid leprosy, BB: Borderline-borderline leprosy or mid-borderline leprosy, BL: Borderline-lepromatous leprosy, and LL: lepromatous leprosy [4]. In the Indian classification (1955) leprosy is divided into six types: Tuberculoid (T), Borderline (B), Lepromatous (L), Indeterminate (I), Maculoanaesthetic (MA) and Polyneuritic (P). Later on, the MA type merged into the Tuberculoid type [5].

NCS is a study of conduction of nerve impulse along the peripheral nerves. It serves as a diagnostic as well as a monitoring tool for leprosy. NCS can detect subclinical neuropathy up to 12 weeks before the clinical neuropathy. So NCS can help in early diagnosis and treatment of leprosy and hence prevention of disability and deformity [6]. However, it is not routinely performed by dermatologists. Previous studies have suggested further research to establish role of NCS in early diagnosis of leprosy neuropathy [6-11]. So, authors intended to do NCS to study the electrophysiological pattern in leprosy patients attending dermatology OPD in a tertiary care centre.

MATERIALS AND METHODS

The present study was a single centre cross-sectional study conducted in the Department of Dermatology at Late Shri Lakhiram Agrawal Memorial Medical College, Raigarh, Chhattisgarh, India, from June 2020 to May 2021. The study was conducted after obtaining approval from the Institutional Ethical Committee (IEC approval number-S.No./Med./Ethics Commi./2021/109). Informed written consent was obtained from all the subjects.

The participants were selected from the patients attending the Skin OPD on the basis of clinical features. The sample size was calculated based on previous studies [11] with confidence interval (CI) of 95% and 80 % power. The patients were classified on the basis of Ridley-Jopling Classification and Indian Classification of Leprosy [4,5].

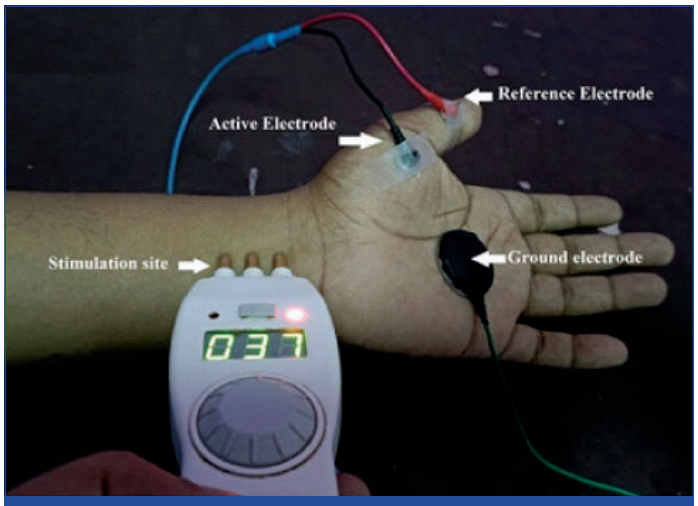
Inclusion criteria: A diagnosed patient of leprosy, classified as TTHD or BTHD or PNL type, willing to participate in the study and aged between 18 years to 60 years were included in the study.

Exclusion criteria: Patients with neuropathy due to other causes such as diabetes, hypothyroidism, neuromuscular diseases, liver

disease, kidney disease, drug induced neuropathy and cases with lepra reaction were excluded from the study.

After obtaining detailed history all the subjects underwent complete physical, motor, sensory and nerve examination. A slit skin smear was done on all patients. NCS were conducted in all the subjects using Allenger's Scorpio Nerve Conduction Velocity-Electro Myography (NCV-EMG) machine at the Department of Physiology according to the standardised protocol [12]. The patients were examined in sitting position for upper limbs and lying on the couch comfortably for lower limbs. The temperature of the room was maintained at 24-28°C. The parameters measured were:

Motor conduction studies: In this distal latency, Compound Muscle Action Potential (CMAP) and nerve conduction velocity were measured in Ulnar, Median, Posterior Tibial and Common Peroneal Nerve. Filters for the study were 2 Hz to 5 kHz with a sweep speed of 2 ms/division. The supramaximal stimulus was obtained with a current of 0-100 mA and stimulus duration of 50-1000 μs. Surface disc electrodes were placed as recording electrodes on abductor pollicis brevis motor point for median nerve [Table/Fig-1], hypothenar eminence for ulnar nerve, midpoint of extensor digitorum brevis for peroneal nerve and slightly anterior/inferior to the navicular tubercle for posterior tibial nerve. Ground electrodes were placed between stimulating and recording electrodes [12].



[Table/Fig-1]: Placement of electrode for median motor nerve studies.

Sensory conduction studies: For this Sensory Latency (SL), Sensory Amplitudes (SNAPs) and Sensory Nerve Conduction Velocities (SNCV) of the median, ulnar and sural nerve were measured. Filters for the study were 20 Hz to 2 kHz with a sweep speed of 2 ms/division. The supramaximal stimulus was obtained with a current of 0-100 mA and stimulus duration of 50-1000 μs. The recording electrode was placed at the index finger slightly distal to MCP for the median nerve, the fifth finger slightly distal to MCP for the ulnar nerve and Posteroinferior to the lateral malleolus for the sural nerve [12].

STATISTICAL ANALYSIS

The quantitative data was represented as their mean±SD. Categorical and nominal data were expressed in percentage. The significance threshold of the p-value was set at <0.05. Data was collected and analysed by unpaired student's t-test using SPSS software version 21.0.

RESULTS

A total of 63 patients between the age group of 18 to 60 years were enrolled for the study out of which 39 (61.9%) were males and 24 (38.1%) were females. The mean age for total patients was 32.26±11.74 years. Out of 63 patients 13 (20.6%) were diagnosed as TTHD, 28 (44.5%) as BTHD and 22 (34.9%) as PNL. Demographic and clinical profile of the patients is shown in [Table/Fig-2].

	Male	Female	Total
Number of Patients	39 (61.9%)	24 (38.1%)	63 (100%)
Age (years)	30.86±11.84	34.58±11.43	32.26±11.74
Age distribution (years)	**(N=39)**	**(N=24)**	**(N=63)**
18-30	23 (58.98%)	9 (37.5%)	32 (50.79%)
31-40	8 (20.51%)	7 (29.17%)	15 (23.81%)
41-50	6 (15.38%)	3 (12.5%)	9 (14.29%)
51-60	2 (5.13%)	5 (20.83%)	7 (11.11%)
Geographical distribution	**(N=39)**	**(N=24)**	**(N=63)**
Urban	21 (53.85%)	9 (37.5%)	30 (47.62%)
Rural	18 (46.15%)	15 (62.5%)	33 (52.38%)
Type of leprosy	**(N=39)**	**(N=24)**	**(N=63)**
TTHD	07 (18%)	06 (25%)	13 (20.6%)
BTHD	16 (41%)	12 (50%)	28 (44.5%)
PNL	16 (41%)	06 (25%)	22 (34.9%)
Duration of disease (months)	**(N=39)**	**(N=24)**	**(N=63)**
<6	16 (41.03%)	08 (33.3%)	24 (38.1%)
6-12	06 (15.38%)	09 (37.5%)	15 (23.8%)
>12	17 (43.59%)	07 (29.2%)	24 (38.1%)

[Table/Fig-2]: Clinical and demographic profile of the patients.

Nerve involvement: Bilateral ulnar, bilateral common peroneal nerve and bilateral posterior tibial nerve of all the patients were examined for nerve thickness. Total 378 nerves were examined out of which 106 (28.1%) nerves were found thickened. The most common nerve found thickened was the ulnar nerve with 52 (41.2%) thickened nerves, 29 (23.1%) common peroneal nerve and 25 (19.8%) posterior tibial nerve was found to be thickened as shown in [Table/Fig-3].

Variables	Thickened nerve	Normal nerve
Ulnar nerve (n=126)	52 (41.2%)	74 (58.8%)
Common Peroneal nerve (n=126)	29 (23.1%)	97 (76.9%)
Posterior Tibial nerve (n=126)	25 (19.8%)	101 (80.2%)
Total (n=378)	106 (28.1%)	272 (71.9%)

[Table/Fig-3]: Distribution of thickened nerves among various nerves in patients of leprosy.

Based on class in TTHD out of 78 nerves only 1 (1.29%) nerve found thickened, in BTHD out of 168 nerves 55 (32.7%) found thickened and in PNL out of 132 nerves examined 50 (37.8%) found thickened as shown in [Table/Fig-4].

Variables	Thickened nerve	Normal nerve
TTHD (78 nerves)	1 (1.29%)	77 (98.71%)
BTHD (168 nerves)	55 (32.7%)	113 (67.3%)
PNL (132 nerves)	50 (37.8%)	82 (62.2%)
Total	106 (28.1%)	272 (71.9%)

[Table/Fig-4]: Distribution of thickened nerves among various class of patients in leprosy.

Electrophysiological profile: On examination of motor nerves latency of ulnar, common peroneal and posterior tibial nerve was increased significantly in thickened nerve as compared to normal nerve. CMAP (Amplitude) and nerve conduction velocity was more affected in thickened nerve as compared to normal nerves and was significantly decreased in ulnar, common peroneal and posterior tibial nerve. Among sensory nerve latency of ulnar and sural nerve significantly increased. Nerve conduction velocity was not affected significantly in ulnar nerve but was significantly decreased in sural nerve [Table/Fig-5].

Peripheral neuropathy: Neuropathy was found in 38 (60.32%) patients [Table/Fig-6]. A total of 20 (90.9%) out of 22 patients having pure neuritic disease had neuropathy, 17 (60.71%) out of 28

patients of BTHD had neuropathy, while 1 (1.29%) out of 13 subjects having TTHD had neuropathy on electrophysiological examination. Most common neuropathy found was of demyelinating sensory and sensorimotor type. Only five patients had pure axonal neuropathy of sensorimotor or sensory nerves. Normal amplitude and latency was observed in 5 (4.72%) out of 106 thickened nerves reduced amplitude and increased latency was seen in 30 (11.03%) out of 272 unthickened nerves.

Nerve	Affected nerve	Normal nerve	p-value
Ulnar motor nerve			
Latency (μs)	3.23±1.84	2.35±0.85	0.002*
Amplitude (mV)	8.74±4.47	10.65±2.36	0.001*
NCV (m/s)	51.20±5.86	54.26±3.24	0.001*
Common peroneal motor nerve			
Latency (μs)	5.31±1.98	3.44±0.95	0.001*
Amplitude (mV)	5.10±2.56	8.56±2.44	0.001*
NCV (m/s)	47.36±7.42	53.26±4.58	0.001*
Tibial motor nerve			
Latency (μs)	4.96±2.12	3.35±1.05	0.002*
Amplitude (mV)	9.16±3.21	13.26±2.74	0.001*
NCV (m/s)	50.23±6.25	53.26±4.25	0.001*
Ulnar sensory nerve			
Latency (μs)	2.65±1.34	1.75±0.92	0.002*
Amplitude (mV)	18.25±5.26	25.32±4.23	0.001*
NCV (m/s)	52.23±4.25	53.26±4.87	0.06
Sural sensory nerve			
Latency (μs)	5.27±2.3	3.26±1.23	0.001*
Amplitude (mV)	42.6±4.56	62.35±5.33	0.001*
NCV (m/s)	49.27±6.39	56.36±4.31	0.001*

[Table/Fig-5]: Electrophysiological profile of various motor and sensory nerve in leprosy. *p<0.05 using unpaired students; t-test was considered to be statistically significant; μs: micro seconds; mV: millivolt; m/s: meter/second; μV: micro volt

S. no.	Type of Neuropathy	Patients (n=63)
1.	Axonal sensorimotor neuropathy	3 (4.76%)
2.	Demyelinating sensorimotor neuropathy	11 (17.46%)
3.	Axonal and Demyelinating sensorimotor neuropathy	12 (19.05 %)
4.	Axonal Sensory Neuropathy	2 (3.17%)
5.	Demyelinating sensory neuropathy	10 (15.87%)
6.	Total Patients with neuropathy	38 (60.32%)

[Table/Fig-6]: Type of neuropathy on electrophysiological diagnosis.

DISCUSSION

The NCS is the single and most important tool to determine nerve function in leprosy. NCS is the study of three parameters of nerve amplitude, latency and velocity [13]. Amplitude represents a summation of activity of the axons within a nerve trunk, latency represents the time taken for nerve stimulus to reach nearest muscle and initiation of muscle contraction and velocity represents the difference in the time taken for the impulse to traverse a measured length of the nerve. NFI can be of demyelinating, axonal, and mixed type. Since lepra bacilli primarily affect Schwann cells which lead to myelination of nerves. The special selectivity for Schwann cells is due to specific binding of mycobacterial antigens {phenolic glycolipid 1 (PGL-1) and laminin-2-binding protein (LBP21)} to the G domain of the laminin a 2-chain. *Mycobacterium leprae* infection leads to nerve damage by -Obstruction of vasa nervorum, interference with Schwann cell metabolism, hypophosphorylation of axonal neurofilaments, immunologic mechanisms like leprosy infected Schwann cells start expressing leprosy antigens with Major Histocompatibility Complex (MHC)-II and thus invite the immunological damage, cell-mediated and immune complex-mediated attack in lepra reaction, cytokine mediated damage from granuloma cells and autoimmune damage, pressure effect in fibro-osseous canals and lastly endoneurial fibrosis leading to irreversible nerve damage. Neuropathy in leprosy is a primarily demyelinating type but later on it eventually evolve to axonal type [14].

In present study, males were more commonly affected than females. Marahatta S et al., also reported male preponderance in their study [7]. In present study, most common nerve found to be thickened was the ulnar nerve, followed by the common peroneal nerve and posterior tibial nerve. Vashisht D et al., and McLeod JG et al., also reported the ulnar nerve most commonly affected nerve [8,9]. The most common neuropathy found was of demyelinating sensory and sensorimotor type. Marhatta S et al., reported 43% of patients having signs of peripheral neuropathy at the time of diagnosis and sensory-motor axonal type as the most common type of neuropathy [7].

The most common motor nerve involved was the ulnar nerve and the most common sensory nerve involved was the sural nerve. Present study findings were consistent with Marahatta S et al., [7]. However, Ramadan WA et al., reported the common peroneal nerve as the commonest motor nerve and the sural nerve as the commonest sensory nerve affected in leprosy [10]. Amplitude and latency were found to be increased in all affected nerves. Nerve conduction velocity was less commonly affected than the other two parameters. Van Brakel WH et al., reported amplitude of sensory nerves and velocity of motor nerves as commonly affected parameters [15]. Reduced nerve conduction velocity in motor nerves was also shown in studies by Jopling WH and Morgan-Hughes JA; Hackett ER et al., [16,17].

Authors found normal amplitude and latency in 5 (4.72%) out of 106 thickened nerves similar to other studies [8,9]. Normal nerve conduction studies can be found in the diseased nerves when only few fascicles of the nerve are affected which have little significance on nerve conduction studies but are evident clinically [18,19]. Reduced amplitude (< 80% of lower limit of normal [20]) and increased latency (>120% of upper limit of normal [20]) was seen in 30 (11.03%) out of 272 unthicken nerves. This was in concurrence with other studies [15,21-23]. Slowing of sensory nerve conduction occurs as early as 12 weeks before other features of leprous neuropathy and tests become abnormal. So, neurological changes can be evident even before clinically evident leprosy.

Limitation(s)

The sample size of study of the present study was small. A similar study on a large scale basis is required to draw some concrete inference.

CONCLUSION(S)

The most common neuropathy found was demyelinating sensory and sensorimotor neuropathy. Ulnar nerve was found to be the most common nerve involved in leprosy. NCS can detect nerve involvement even when it is not apparent clinically. So NCS should be included in routine clinical practice in leprosy to determine the degree of nerve involvement and monitoring of ongoing treatment.

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