Original Research Article

Clinical study of nerve function impairment in newly diagnosed leprosy patients at a tertiary care center in Shahjahanpur district

Amar Singh¹*, Astha Pant²

¹Department of Dermatology, Venereology and Leprosy, Autonomous State Medical College, Shahjahanpur, Uttar Pradesh, India
²Department of Dermatology, Government Combined Hospital, Dehradun, Uttarakhand, India

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*Correspondence:
Dr. Amar Singh,
E-mail: dr.amar13hims@gmail.com

ABSTRACT

Background: In leprosy nerve function impairment may result from pathological and immunological processes that take place in peripheral nerves. Prevalence rate of leprosy in India is 0.81 per 10,000 populations. The study was undertaken to determine the status of nerve function impairment at the time of registration for therapy in new leprosy patients.

Methods: History of the patients was taken and clinical examinations were performed and they were assisted for nerve function impairment by performing sensory test and voluntary muscle power.

Results: The most commonly affected nerve by function impairment was the posterior tibial, followed by the ulnar nerve. In the present study 29% patients had grade 1 disability and 10% had grade 2 disabilities.

Conclusions: The loss of nerve function and incapacitating deformities occurring in a small proportion of leprosy patients result in serious social and psychological impact in their quality of life. Therefore, early detection of nerve function impairment is needed to avoid complications and better management of leprosy.

Keywords: Nerve function impairment, Neuropathy, Disability

INTRODUCTION

Leprosy is a chronic granulomatous infectious disease caused by Mycobacterium leprae, which usually affects the peripheral nerves and the skin.¹ It might affect the eye, the mucosa of the upper respiratory tract, muscle, bone and testes.² Nerve function impairment (NFI) may result from pathological and immunological processes taking place in peripheral nerves. These include the presence of Mycobacterium leprae in the nerve, trauma, oedema causing increased intraneural pressure, vascular changes, and hypersensitivity granuloma.³ Reactive episodes are widely accepted as common causes of NFI.⁴ Nerve involvement in leprosy affects sensory, motor and autonomic function of peripheral nerves.⁵ As a result of anaesthesia of skin and muscle weakness are the major causes of disability and mutilations. Nerve damage may be present at the time of diagnosis and can occur during and after adequate treatment with multiple drug therapy.⁶

Around 10% of new leprosy cases registered every year have signs of sensory, motor or autonomic neuropathy at diagnosis.⁷ Sensory loss is the earliest and most frequently affected modality but a predominantly motor loss can also occur. The nerves most likely to be involved are the mixed nerve trunks of the upper and lower extremity, especially in those segments where the nerve is subcutaneous and has a cooler temperature. These include great auricular nerves in the neck, the supraclavicular nerves as they cross the clavicles, the ulnar nerves just the elbows, the radial nerve at the spiral groove, the median nerves at the wrist, the radial cutaneous nerve in the lower forearm, the lateral popliteal nerves as they wind round the necks of fibulae, the
posterior tibial nerves behind the medial malleoli and the superficial peroneal nerves in front of the ankles and on the dorsa of the feet.9

Mechanism of nerve injury

Four related aspects of nerve injury in leprosy must be considered in understanding the pathogenesis of neuritis in leprosy: localization of M. leprae to peripheral nerves, infection of Schwann cells (SCs), immunologic responses, and inflammation.

The first essential step in leprosy neuritis is the localization of M. leprae to peripheral nerves. Several steps are required for the ultimate entry of M. leprae into Schwann cells. In the second step M. leprae specifically binds to α-dystroglycan in the presence of the G domain of the α2 chain of laminin-2.9 Finally, the immune response may also be directed at M. leprae-infected SCs. Infected SCs are also able to process and present antigen to T cells, and thus may become targets of immune responses. As a long-term consequence of these and other, unknown mechanisms, SCs are ultimately functionally impaired or destroyed in infected nerves. The end result is a demyelination neuropathy.10

Pattern of neuropathy

Peripheral neuropathy in tuberculoid leprosy: Nerve damage in tuberculoid leprosy is usually asymmetrical. Granulomatous inflammation of peripheral nerves causes palpable enlargement, which may or may not be painful and causes sensory and motor loss in the distribution of the affected nerve.11

Peripheral neuropathy in lepromatous leprosy: It is characterized by more widespread involvement of skin and nerves causing slow, progressive, bilateral, symmetrical, distal polyneuropathy leads to a glove and stocking neuropathy; peripheral nerves involvement tends to occur late.12

Peripheral neuropathy in borderline leprosy: When the clinical illness is toward the tuberculoid spectrum (BT), there may be a single lesion with asymmetrical nerve involvement, but as the disease moves toward the lepromatous pole (BL) multiple symmetrical skin and nerve lesions may be seen.12

Pure neural leprosy: The concept of a form of leprosy with one or more enlarged peripheral nerves, but no skin lesions, seems to be well established by experienced observers, especially in India.12 Most of these patients present with a clinical picture consistent with mononeuritis multiplex.

Silent neuritis: Ongoing nerve damage can occur in the absence of symptoms. Silent neuritis shows persistence of M. leprae or its antigens in Schwann cells, progressive intraneural oedema, and advancing restrictive fibrosis with progression of neurological deficit.13

Eye involvement: Lagophthalmos usually results in damage to the zygomatic and temporal branches of the facial nerve. It gives rise to exposure keratopathy. Reduced corneal and conjunctival sensation due to involvement of the ophthalmic branch of the trigeminal nerve predisposes to corneal ulceration.14

This study was designed to evaluate the status of nerve function impairment at the time of registration for therapy in new leprosy patients. In this study we evaluate relation between various types of leprosy and leprosy reactions with nerve function impairment and disability.

METHODS

It was a hospital based cross-sectional descriptive study which was conducted in Department of Dermatology, Venereology and Leprosy, Autonomous State Medical College, Shahjahanpur, Uttar Pradesh, India. The total number of new cases seen in the OPD from April, 2019 to April 2020 was 53900 and the calculated prevalence of leprosy for these 12 months was 0.94. A sample size of 300 was taken for the study.

Inclusion criteria

All newly diagnosed leprosy patients attending to OPD were included.

Exclusion criteria

Anyone unwilling to give consent, individuals who had started anti leprosy drug from other hospital, any known case of diabetes mellitus and other neurological disorders.

Criteria of impairment

NFI is defined as ‘clinically detectable impairment of motor, sensory or autonomic nerve function.15 Sensory NFI was defined as reduction by 2 points or more in the sensory score of any one nerve’s distribution, as tested by ballpoint pen at standard test sites. Motor NFI was defined as reduction by 2 points or more in the Medical Research Council (MRC) grade of movement tested.14

Impairment status was assessed as WHO disability grading system (0, 1, 2), according to WHO disability grading 1998.16

For hands and feet

- Grade-0: No anaesthesia, no visible deformity or damage.
- Grade-1: Anaesthesia present, no visible deformity or damage.
- Grade-2: Visible deformity or damage present.
For eyes

- **Grade-0**: No eye problems due to leprosy; no evidence of visual loss.
- **Grade-1**: Eye problem due to leprosy present, but vision not severely affected as a result (vision 6/60 or better; can count fingers at six meters).
- **Grade-2**: Severe visual impairment (vision worse than 6/60; inability to count fingers at six meters), lagophthalmos, iridocyclitis and corneal opacities.

Sensory testing

Sensory testing was checked with Semmes-Weinstein monofilaments. Trigeminal, ulnar, median and posterior tibial nerves on each side. The monofilaments used were 2 gm for the hand and 10 gm for the feet. Normal reference values were 200 mg for the hand and 2 gm for the foot (excluding the heel). Corneal sensation with cotton wool, if required. The sensory testing of palms was tested using a monofilament giving a force of 2 gm and of soles using 10 gm when pressed until it bent. The test first explained to the patient and demonstrated on a skin area with normal sensibility. Then the patient was asked to close his eyes and the monofilament was applied to the different test sites in random order until each site had been tested. The test sites and records on the diagram of the hands and feet the result of the monofilament testing at each test site (Figure 3 and 4).

Voluntary motor testing

Assessment of facial, ulnar, radial, median and lateral popliteal nerves of both hands and feet was done by using the MRC grading of muscle power (Table 1 and 2).

Score was derived for each nerve.
The majority of cases (59%) presented to the hospital voluntarily. The median duration of symptoms at presentation for the illiterates and literates were 11.5 and 7.0 months respectively, which was however not significant statistically (Mann-Whitney test, p value = 0.308). However, literates cited lack of manpower being the cause of the delay more often than the illiterates (22.1% vs. 12.5%).

Most of the lesions consisted of plaques in 129 (43%) cases. This was followed by macules in 84 (28%), infiltration in 12 (4%), ulcer in 18 (6%), nodule in 54 (18%), and infiltration in 12 (4%) patients. 18 (6%) patients were presented without any skin lesions.

Table 3: Grading of impairment in new patients.

<table>
<thead>
<tr>
<th>Impairment grades</th>
<th>WHO categorization</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MB (%)</td>
<td>PB (%)</td>
</tr>
<tr>
<td>Impaired</td>
<td>66 (39.3)</td>
<td>51 (38.6)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>54 (32.1)</td>
<td>33 (25.0)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>12 (7.2)</td>
<td>18 (13.6)</td>
</tr>
<tr>
<td>Grade 0</td>
<td>102 (60.7)</td>
<td>27 (61.3)</td>
</tr>
<tr>
<td>Total</td>
<td>168 (100.0)</td>
<td>78 (100.0)</td>
</tr>
</tbody>
</table>

Out of 300 patient 120 (40%) were BTHD, 75 (25%) LLHD, 51 (17%) BLHD, 24 (8%) TTHD, 21 (7%) PNHD and 9 (3%) cases were BBHD. Out of 300 cases

Table 1: Voluntary muscle test: MRC modified grading of muscle power.

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 Right facial</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C2 Left facial</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C3 Right ulnar</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C4 Left ulnar</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C5 Right median</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C6 Left median</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C7 Right radial</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C8 Left radial</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C9 Right lateral popliteal</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
<tr>
<td>C10 Left lateral popliteal</td>
<td>MRC=5</td>
<td>MRC=4</td>
<td>MRC=3</td>
<td>MRC&lt;3</td>
<td></td>
<td></td>
<td>Score</td>
</tr>
</tbody>
</table>

Table 2: MRC modified grading of muscle power.

<table>
<thead>
<tr>
<th>Score</th>
<th>Muscle response</th>
<th>Severity scale score</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Full range of movement (FROM)</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>FROM but less than normal resistance</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>FROM but no resistance</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Partial range of movement with no resistance</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>Perceptible contraction of the muscle not resulting in joint movement</td>
<td>3</td>
</tr>
<tr>
<td>0</td>
<td>Complete paralysis</td>
<td>3</td>
</tr>
</tbody>
</table>

RESULTS

The age distribution of the patients varied between 9-75 years. The mean age±SD was found 37.75±18.22 years. The majority of the cases were between the age groups of 15 to 24 year, followed by 25 to 34 years. Out of 300 patients 7% were ≤15 years of age, and 1% was ≥ 65 years of age. Among the total 300 cases, there were 237 males and 63 females. M:F ratio was 3.76:1.

The first symptom is skin lesion in 228 (76%) of cases, sensory changes in 63 (21%) of cases whereas motor impairment is found only in 9 (3%) of cases.

Majority of the case (44%) were registered within 6 months period (among them 15% patients had come within 3 months of the symptoms); only 4% of the cases came after ≥5 years of symptoms. Lack of awareness was the main reason for delay for treatment. There educational status was 32% illiterate, 32% primary level, 22% secondary level and 14% higher secondary level.

The majority of cases (59%) presented to the hospital voluntarily. The median duration of symptoms at presentation for the illiterates and literates were 11.5 and 7.0 months respectively, which was however not significant statistically (Mann-Whitney test, p value = 0.308). However, literates cited lack of manpower being the cause of the delay more often than the illiterates (22.1% vs. 12.5%).

Most of the lesions consisted of plaques in 129 (43%) cases. This was followed by macules in 84 (28%), infiltration in 12 (4%), ulcer in 18 (6%), nodule in 54 (18%), and infiltration in 12 (4%) patients. 18 (6%) patients were presented without any skin lesions.

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52 cases were slit skin smear for AFB were positive and remaining cases were negative.

Among 300 patients 168 (44%) were PB and 132 (56%) were MB. 62 patients had thickened peripheral nerve trunks. In 300 patients, 150 (50%) patient presented with thickened, non tender, 36 (12%) had thickened and 114 (38%) patient had no nerve thickening.

Nerve function impairment was present in 117 (39%) cases at the time of diagnosis. 66 MB patients and 51 PB patients had impairment at time of registration (Table 3).

### Table 4: Relation between impairment and type of leprosy.

<table>
<thead>
<tr>
<th>Type of leprosy</th>
<th>Impairment grading</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>N (%)</td>
</tr>
<tr>
<td>BB</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>BL</td>
<td>36 (70.6)</td>
</tr>
<tr>
<td>BT</td>
<td>72 (60.0)</td>
</tr>
<tr>
<td>LL</td>
<td>48 (64.0)</td>
</tr>
<tr>
<td>PN</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>TT</td>
<td>21 (87.5)</td>
</tr>
</tbody>
</table>

![Nerve involvement in leprosy patients](image)

**Figure 5: Prevalence of impairment at first registration in individual nerves in 100 new leprosy patients.**

s=sensory, m=motor.

39 patients had neurological involvement at the time of registration, among them 20 cases had both sensory and motor involvement. 24 BTHD patients had grade 1 impairment and 4 BTHD patients had grade 2 impairment (Table 4). 45 BT, 33 BLHD patients had reversal reaction and 42 LLHD patients had type 2 reaction.

The most commonly affected nerve by function impairment was the posterior tibial (sensory), followed by the ulnar nerve (Figure 6A and B).

**Figure 6: (A) Clawing of fingers and multiple ulcers in anaesthetic hand, (B) trophic ulcer with dry hyperkeratotic cracked foot.**

### DISCUSSION

About 33-56% of newly registered leprosy patients already have clinically detectable nerve function impairment (NFI), often no longer amenable to MDT. Unfortunately, many patients are diagnosed late and are at greater risk of developing the reactions and neuritis. If these reactions are treated effectively, early nerve damage can be reversed and disability can still be prevented.19

In this study higher number of patients was found in the age groups 15 to 24 years. The mean age of the patients was found to be 37.75 (SD±18.229) years. It is almost similar to Robertson’s finding (mean age 35.9 years).20

Childhood leprosy accounted for 7% of all leprosy patients in the present study, which is similar to Sardana’s finding (7.71%).21

In this study the percentage of males 79% exceeded that of females 29%. In general, leprosy had been more prevalent in males than females in different studies.20,22

Based on the clinical features the most common morphological presentation of the lesions was plaques in 43% of patients, followed by macular lesion seen in 28% of patients. The skin lesions are outnumbered similar to
most of the published studies. In a study, Meima et al found that 46% of patients were slit skin smear positive which is lower than current study (52%). In this study the number of multibacillary cases exceeded that of paucibacillary patients, so that 56% of the patients had multibacillary leprosy which similar (55.13%) to report of Government of India.

In the present study 300 patients were enrolled, among them the prevalence of sensory impairment was a little higher than motor impairment. Sensory impairment of the posterior tibial nerve was the most commonly affected in 20% patients, followed by ulnar nerve 19%, and median nerve 13%. Motor impairment of the ulnar nerve was found in 19% of the patients; followed by lateral popliteal nerve 6%, median nerve 5%, facial nerve 1% and radial nerve 1%.

There is considerable variance between the results due to differences in methods of testing and criteria for selection of patients. Magora et al and Brown et al measured nerve conduction velocity, Brunel et al used the point discrimination test to measure sensibility, while the other authors used manual muscle tests and either a ball pen or monofilaments to test sensibility. The prevalence of sensory impairment of ulnar, median, lateral popliteal and posterior tibial found by Becx-Bleumink et al was understandably higher than in the present study since they report on a selective group of treated patients with nerve function impairment. Brown et al, testing with nylon monofilaments, reported a prevalence of sensory impairment of 29% for ulnar and 13% for median nerves, which is than present study. The prevalence of motor impairment found by Magora et al was higher than in current study since they performed motor nerve conduction velocity testing. In the present study motor impairment of lateral popliteal, median and facial nerves is higher than reported by Brakel et al. Croft et al found that the most commonly affected nerve by function impairment was the posterior tibial (sensory) followed by the ulnar nerve. In the present study 29% patients had grade 1 disability and 10% had grade 2 disability. Meima et al (31% grade 1 and 23% grade 2 in 592 patients) and De Oliveira et al (35% grade 1 and 14% grade 2 in 5350 patients) found that higher percentage of disability in comparison to current study. Croft et al (9.61% grade 1 and 5.97% grade 2) found that lower percentage of disability in comparison to present study.

In several studies, the WHO disability grading has been used to evaluate and monitor patients’ ‘disabilities’ while on treatment. Low prevalence rates of impairment in new patients at the time of diagnosis are interpreted as an indication of early case reporting. This may be the result of improved health services or raised community or professional awareness. Delayed presentation is a recognized risk factor for disability in leprosy. Meima et al showed a heavy impact of long registration delay on the impairment status of new leprosy patients from central Ethiopia. In the present study majority of the case (44%) were registered within 6 months period (among them 15% patients had come within 3 months of the symptoms); only 4% of the cases came after ≥5 years of symptoms. Lack of awareness was one of the reasons for delayed presentation. Nicholls et al suggested that a threshold defining early presentation (e.g. less than 6 months) could be used as an indicator for good practice in leprosy control.

CONCLUSION

The present hospital-based study was conducted to show the clinical and epidemiological characteristics and nerve function impairment in new leprosy patients. The loss of nerve function and incapacitating deformities occurring in a small proportion of leprosy patients result in serious social and psychological impact in their quality of life. Therefore, early detection of nerve function impairment and proper management is very important.

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Ethical approval: The study was approved by the institutional ethics committee

REFERENCES


