Leprous Neuropathy: Observational Study Highlighting the Role of Electrophysiology in Early Diagnosis

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Abstract

Background Worldwide leprosy is a common cause of peripheral neuropathy. Electrophysiology is underutilized in its diagnosis.

Objective This study aims to evaluate the usefulness of electrophysiological study in the diagnosis of leprous neuropathy.

Materials and Methods Clinical and electrophysiological abnormalities of 36 histopathology proven leprosy patients from January 2015 to January 2017 were studied.

Statistical Analysis Proportions were compared by Chi-square test.

Results Total patients were 36. Thirty-four patients had abnormal electrophysiology and 34 had neurological deficits like weakness, sensory changes, and thickening. By clinical examination, multiple nerve involvement (motor weakness, sensory changes, and nerve thickening) occurred in 29, single nerve in 5, and no nerve involvement in 2. With electrophysiology, multiple nerve involvement (mononeuritis multiplex) was present in 32, single nerve in 2, and normal conduction parameters in 2. From the 36 patients, a total of 1,008 nerves were subjected to clinical examination and 132 were picked up clinically as affected, (13.1%). Electrophysiological study was done in 504 nerves, and 215 were found to be involved, (43%). Nerve abnormality detected by electrophysiology is significantly higher than clinical detection. (Chi-square =164.4054; p = 0.0000). Clinically, the most commonly affected nerve was unar (27) and the least affected was median (2) nerve. Electrophysiology detected 69% of nerves with demyelination and 35% of nerves with axonal features (mosaic pattern).

Discussion There was subclinical neuropathy with electroclinical dissociation, as evidenced by more abnormality in electrophysiology than clinical examination. The nerve involvement was mononeuritis or mononeuritis multiplex pattern, both clinically and electrophysiologically. Electrophysiology showed both axonal and demyelinating nerve involvement (mosaic pattern). All the three features are present in leprous neuropathy. In corollary, if a patient has these electrophysiological features, he should be thoroughly investigated for leprosy.

Conclusion Triple findings, such as subclinical neuropathy with electroclinical dissociation, mononeuritis multiplex, and mosaic pattern of demyelination and axonopathy, suggest leprous neuropathy.

Keywords ► leprous neuropathy ► electrophysiology ► nerve conduction study ► subclinical ► electroclinical dissociation ► mosaic pattern ► mononeuritis multiplex

DOI https://doi.org/10.1055/s-0041-1727575
ISSN 0976-3147

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Thieme Medical and Scientific Publishers Pvt. Ltd. A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Published online: 2021-06-16
Introduction

Globally, before diabetic neuropathy, leprosy was the commonest peripheral nerve disorder and people of countries like India and Brazil were deformed and disabled due to it. Due to significant peripheral nerve involvement, leprosy became a stigmatizing public health issue of great dimension. In leprosy, cutaneous manifestation aids in early identification and neural deficits causes disability and stigma. Early detection and treatment prevents disability and deformity. Disability due to leprosy is common with 3 million people suffering worldwide. Projections of global leprosy burden estimated 5 million new cases to occur between 2000 AD and next 20 years, with 1 million fresh grade-2 (severe) disabilities.

Though leprosy affects both central and peripheral nervous system, peripheral nerves are commonly involved. Neuropathy affects motor, sensory, and autonomic divisions of peripheral nervous system. Clinical examination was the corner stone of suspecting and diagnosing leprosy with confirmation by skin and ear lobe smear examination. Intense vigilance and the National Leprosy Eradication Program (NLEP) measures lead to elimination of leprosy by 2005 in India, but eradication is still a dream. In some states of India, current prevalence exceeded elimination point with rising child hood cases. In India, between time periods, 2006 to 2015, prevalence was 5.9 and 11.2% in Kerala and Karnataka, respectively, among children. Children have increased susceptibility to leprosy due to their lack of immunity and exposure to patients within family. The proportion of children among new cases indicates continued disease propagation. Electrophysiology features of leprous neuropathy were initially outlined in the 1960s. By the 1970s, details of electrophysiological abnormalities became more clear. Though many characteristic features were described till date, even today, it is not utilized for diagnosis and prognosis. Many reasons prevented routine use of electrophysiology in diagnosing and prognosticating leprous neuropathy. Factors, like stable temperature and electrical supply required for the machine, can be overcome by temperature controlled cabin vans with unlimited power supply aided by solar energy. Other reasons like very costly equipment and technical expertise had changed in recent times.

Objective

This study was aimed to determine the clinical and electrophysiological features of leprous neuropathy, so that it can be diagnosed early and accurately with the available aids.

Materials and Methods

Clinical and electrophysiological abnormalities in 36 histopathology proven leprosy patients between January 2015 and January 2017 in the age group of 5 to 69 years (27 males and 9 females) were studied.
of electrophysiology (Chi-square = 9.0017; p = 0.0026). Seventy-two median nerves were palpated but only two were thickened. Electrophysiology showed 33 sensory abnormalities (Chi-square = 33.92; p = 0.000) and 10 motor abnormalities (Chi-square = 4.4545; p = 0.034) in median nerve. These differences were statistically significant (Table 2).

Clinically, 29 patients had mononeuritis multiplex (including sensory and motor), 5 mononeuritis, and 2 were without nerve involvement. With electrophysiology, 32 patients had mononeuritis multiplex, 2 mononeuritis, and 2 normal conduction parameters.

Addressing the fraction of demyelination and axonopathy in the patients, 146 out of 215 (68%) had demyelination, while 77 (36%) had axonopathy. There were overlaps in the electrophysiology findings as shown in Table 2.

### Discussion

Three clinical and electrophysiological features noticed in the series of 36 patients are as follows:

1. Subclinical neuropathy (electroclinical dissociation).
2. Mononeuritis multiplex or mononeuritis (clinically and electrophysiologically).
3. Mosaic pattern of combined demyelinating and axonal changes (in electrophysiology).

**Subclinical Neuropathy (Electroclinical Dissociation)**

Subclinical neuropathy was evidenced by more nerve abnormalities detected by electrophysiology than clinical examination and was statistically significant (exception in two patients). Clinically unaffected nerves had reduced amplitudes than conduction velocities. Thus electroclinical dissociation was noticed by the 1990s. The dissociation between clinical examinations of various types and testing was analyzed with NCS as gold standard. Dissociation with reduced sensitivity to nerve palpation was present in median, ulnar, great auricular, and common peroneal nerves. In the current study, electroclinical dissociation was present in all nerves tested except peroneal sensory.

In considering those with electroclinical dissociation, 34 patients each had abnormal electrophysiology and clinical examination. The number of patients tested normal with regard to either clinical or electrophysiology were

<table>
<thead>
<tr>
<th>Nerve type tested</th>
<th>Nerves examined clinically</th>
<th>Clinically abnormal (thick)</th>
<th>Total nerves tested-EP</th>
<th>EP abnormal nerves</th>
<th>Clinical/EP comparison (Chi-square)</th>
<th>p-Value</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total nerves</td>
<td>1,008</td>
<td>132</td>
<td>504</td>
<td>215</td>
<td>164.40</td>
<td>0.0000</td>
<td>Yes</td>
</tr>
<tr>
<td>Ulnar sensory</td>
<td>72</td>
<td>27</td>
<td>72</td>
<td>46</td>
<td>9.0019</td>
<td>0.0027</td>
<td>Yes</td>
</tr>
<tr>
<td>Ulnar motor</td>
<td>72</td>
<td>27</td>
<td>72</td>
<td>38</td>
<td>2.8043</td>
<td>0.0940</td>
<td>No</td>
</tr>
<tr>
<td>Median sensory</td>
<td>72</td>
<td>2</td>
<td>72</td>
<td>33</td>
<td>33.920</td>
<td>0.0000</td>
<td>Yes</td>
</tr>
<tr>
<td>Median motor</td>
<td>72</td>
<td>2</td>
<td>72</td>
<td>10</td>
<td>4.4545</td>
<td>0.0348</td>
<td>Yes</td>
</tr>
<tr>
<td>Sural</td>
<td>72</td>
<td>9</td>
<td>72</td>
<td>14</td>
<td>0.8279</td>
<td>0.3628</td>
<td>No</td>
</tr>
<tr>
<td>Peroneal sensory</td>
<td>72</td>
<td>15</td>
<td>72</td>
<td>16</td>
<td>0.0411</td>
<td>0.8393</td>
<td>No</td>
</tr>
<tr>
<td>Peroneal motor</td>
<td>72</td>
<td>18</td>
<td>72</td>
<td>26</td>
<td>1.603</td>
<td>0.2600</td>
<td>No</td>
</tr>
<tr>
<td>Posttibial</td>
<td>72</td>
<td>9</td>
<td>72</td>
<td>32</td>
<td>16.502</td>
<td>0.0000</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Abbreviation: EP, electrophysiological.
equal (two). But the number of nerves identified as abnormal was more with electrophysiology. Chance for missing diagnosis of leprosy was there in this series if clinical examination alone was used. Clinical examination did not reveal pathology of several nerves and two patients. With electrophysiology alone, there was a chance for missing diagnosis in two patients. This will not occur in real-life situation. Electrophysiology will be used only as an additional aid after clinical examination.\(^1\) When both are combined, all patients and neural abnormalities could be detected as evidenced from this series. Thus as a single test, electrophysiology is better, but combination of clinical examination and electrophysiology is the best approach.\(^2\) When sympathetic skin response (SSR) was combined with routine electrophysiology, features of nerve dysfunction identified was 81.8%, as it will identify small fiber involvement. In the current study, SSR was not done, as it required more expertise and time consumption. Our aim was to know the electrophysiological abnormalities with routine nerve conduction tests by a regular technician with minimum time consumption, so that it can be used in the rural society (field setting).

### Mosaic Pattern of Neuropathy\(^2\)
Electrophysiological abnormalities were neither purely demyelinating nor axonal. It was mosaic pattern of 68% demyelinating and 36% axonal with overlap.\(^1\) Electrophysiological abnormalities reported were reduced amplitude of motor and sensory potential (axonopathy) or prolonged latencies and slowing of conduction velocity (demyelination).\(^3\,\(^8\) Different authors have found varying pattern of neurophysiological abnormalities in leprous neuropathy. Electrophysiological changes recognized in the 1970s were predominantly conduction slowing of motor nerves in early disease and reduced amplitudes in clinically advanced cases.\(^9\,\(^1\)\) It is now known that sensory nerves are identified to be involved in the early disease phase.\(^1\) Certain investigators were of the opinion that sensory nerve action potential (SNAP) and compound nerve action potential (CNAP) amplitudes were more suggestive of early neuropathy than slowing of velocity.\(^1\) In another study, sensory conduction velocity was found to be slow.\(^2\) Axonopathy of motor nerves are described. Electromyography showed denervation of small muscles of hand which indicated axonopathy of ulnar nerves.\(^2\) But before symptom onset of neuropathy, there is conduction slowing in sensory and motor nerves. Thus, short demyelinating and axonal changes (mosaic pattern)\(^3\) can be seen, in leprous neuropathy, as it is seen in the current series. Here, in most nerves, the abnormality was predominantly demyelination, while in peroneal motor and sensory and sural nerves, it was predominantly axonopathy.\(^6\,\(^7\) In another study, 98% had electrophysiological abnormalities. They found reduction of SNAP and compound muscle action potential (CMAP) to be the earliest and commonest change.\(^2\) Thus, a mosaic pattern peripheral neuropathy points to leprosy neuritis by electrophysiology.

### Mononeuritis Pattern
Motor weakness in nerve distribution was present in 17 patients. Clinical peripheral nerve involvement is shown in Tables 1 and 2. Thus both clinically and electrophysiologically, pattern was mononeuritis/mononeuritis multiplex.\(^2\) Mononeuritis multiplex occurs most commonly due to leprosy and systemic vasculitis.\(^2\) Leprosy is the disease with skin lesions and mononeuritis of small sensory nerves, later involving motor trunks. Thus it produces mononeuritis or mononeuritis multiplex. When mononeuritis is caused by vasculitis, it is axonal; whereas in leprosy, histopathology and electrophysiology characterize more of motor demyelinating neuropathy. There is also conduction block.

Thus, when the electrophysiology shows subclinical neuropathy with electroclinical dissociation in a mononeuritis or mononeuritis multiplex type of nerve involvement and mosaic pattern of both demyelination and axonal changes, in an endemic area, with or without contact history, one should strongly consider and rule out leprosy and leprous neuropathy. Even in a person with peripheral neuropathy without

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**Table 3** Electrophysiological changes in nerves

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Nerve tested</th>
<th>Nerves with increased latency (demyelination) n (%)</th>
<th>Nerves with reduced amplitude (axonopathy) n (%)</th>
<th>Nerves with decreased velocity (demyelination) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ulnar sensory</td>
<td>24/46 (52)</td>
<td>12/46 (26)</td>
<td>33/46 (72)</td>
</tr>
<tr>
<td>2</td>
<td>Ulnar motor</td>
<td>24/38 (63)</td>
<td>5/38 (13)</td>
<td>29/38 (76)</td>
</tr>
<tr>
<td>3</td>
<td>Median sensory</td>
<td>24/33 (73)</td>
<td>6/33 (18)</td>
<td>29/33 (88)</td>
</tr>
<tr>
<td>4</td>
<td>Median motor</td>
<td>8/10 (80)</td>
<td>0/10 (0)</td>
<td>10/10 (100)</td>
</tr>
<tr>
<td>5</td>
<td>Sural</td>
<td>10/14 (71)</td>
<td>9/14 (64)</td>
<td>5/14 (36)</td>
</tr>
<tr>
<td>6</td>
<td>Peroneal sensory</td>
<td>10/16 (63)</td>
<td>13/16 (81)</td>
<td>9/16 (56)</td>
</tr>
<tr>
<td>7</td>
<td>Peroneal motor</td>
<td>9/26 (35)</td>
<td>13/26 (50)</td>
<td>11/26 (42)</td>
</tr>
<tr>
<td>8</td>
<td>Posterior tibial</td>
<td>9/32 (28)</td>
<td>9/32 (28)</td>
<td>17/32 (53)</td>
</tr>
<tr>
<td>9</td>
<td>Total nerves</td>
<td>118/215 (54.8)</td>
<td>67/215 (35.8)</td>
<td>143/215 (67.9)</td>
</tr>
</tbody>
</table>
contact history, if electrophysiology suggests all three features, that is, subclinical neuropathy (electroclinical dissociation), mosaic pattern of demyelination, and axonopathy in mononeuritis or mononeuritis multiplex distribution, one should strongly consider leprosy neuritis. This approach of incorporating electrophysiology for diagnosing neuropathy in leprosy at a very early stage will help in reducing the disability and deformity.

**Conclusion**

Use of electrophysiology in leprosy will enable early detection of neuropathy, prompt treatment, and prevention of disability and stigma. Nerve conduction study (electrophysiology) is of great help in identification of neuropathy in new cases, (enabling zero disability) follow-up of known cases will definitely contribute toward a near-total freedom from disability among leprosy patients.

**Conflict of Interest**

None declared.

**References**