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Original Article

# The Relationship of Nerve Function Impairment and Symptoms in Leprosy

MGB do Nascimento[1], GL Lopes[2], NC Albuquerque[3], DN Somensi[4], MB Xavier[5]

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The evaluation of the neurological function of leprosy patients is very important for the early dignosis and treatment of nerve damage. This study aims to correlate the reported symptoms with sensory and motor findings of neurological assessment in upper and lower limbs of leprosy patients. An analytical cross-sectional study was carried out at a specialized leprosy service in Belém, Pará, Brazil. This study included 97 leprosy patients treated between 2014 and 2015. Assessment included nerve palpation, voluntary muscle test, sensory testing in hands and feet with Semmes-Weinstein monofilaments, in addition to the recording of symptoms reported by the patient. Data analysis was performed using the chi-square test, G test, t test and Spearman correlation test, considering the alpha significance level of 0.05. Of the 97 leprosy patients, 77 (79.4%) had symptoms, the most common were those related to sensory fibers, including pain and numbness were the most mentioned. The patients with symptoms had more advanced sensory damage stages, higher degree of disability in the lower limbs and motor damage occuring more frequently. The health professionals should be alert to patients with symptoms, allocating more attention at the time of evaluation in order to better prevent / manage disabilities.

**Keywords :** Leprosy, *Mycobacterium leprae*, Neuritis, Symptoms, Sensory - Motor Damage

## Introduction

The leprosy, even though curable, it is still an endemic disease in many countries, especially the tropical climate. Even after the significant decline due to the implementation of treatment with multidrug therapy (MDT) the numbers are still alarming. In the year 2016, World Health Organization (WHO) recorded 214 783 new cases of the disease, with significant contribution from Brazil, which persists as the second most endemic country in the world, losing only to India (WHO 2017). Over the years, many control strategies

[1] MGB do Nascimento, Master of Science, Núcleo de Medicina Tropical, Universidade Federal do Pará, Belém, Pará, Brazil.
[2] GL Lopes, Master of Science, Núcleo de Medicina Tropical, Universidade Federal do Pará, Belém, Pará, Brazil.
[3] NC Albuquerque, Master of Science, Núcleo de Medicina Tropical, Universidade Federal do Pará, Belém, Pará, Brazil.
[4] DN Somensi, Master of Science, Additional Professor, Centro de Ciências Biológicas e da Saúde, Universidade do Estado do Pará, Belém, Pará, Brazil.
[5] MB Xavier, Doctor of Science, Professor, Núcleo de Medicina Tropical, Universidade Federal do Pará. Centro de Ciências Biológicas e da Saúde, Universidade do Estado do Pará, Belém, Pará, Brazil.
**Address :** Nucleus of Tropical Medicine. AV. Generalíssimo Deodoro, nº 92, Umarizal, Belém, Pará-Brazil. 66055-240
**Corresponding author :** Mariana Garcia Borges do Nascimento **e-mail:** marianaglborges@gmail.com

have been developed in an attempt to contain the spread of this disease. Recently, the control strategy for leprosy implemented by national programmes of endemic countries for the five-year period 2011-2015, sought to reduce the overall rate of new cases with disability grade (GI) equal to two per 100 000 inhabitants in at least 35% by the end of 2015, compared to the baseline at the end of 2010 accounted for 1.2 cases per 100 thousand inhabitants (WHO 2009).

The majority of damage, disability and deformities in leprosy occur as a consequence of a neural impairment, due to the preference of *Mycobacterium leprae* by skin cells and the peripheral nervous system (Schwann cells) (Silva 1960). Therefore, the routine of neurological assessment of these patients plays a fundamental role in the leprosy follow-up, since it allows a better knowledge of the damage caused and, consequently, a timely action of the health team to avoid progressive and permanent loss of the nerve (Leite et al 2010). In this regard, Ministry of Health of Brazil recommends in the Disability Prevention Manual, 2001, the use of simplified neurological assessment, consisting of assessment tools of sensory and motor function reliable and validated for this routine (Van Brakel et al 1996, Anderson & Croft 1999, Ministério da Saúde do Brasil 2001). However, despite having validated instruments, the health professional should be aware of the care in the interpretation of the tests, because, in most cases, have a subjective character and suffer various external interference. In general, the literature indicates that the sensitivity for the diagnosis of leprosy is greater when they are interpreted together, including in the clinical perspective (Kaplan & Gelber 1985, Garbino & Opromolla 2003, Ministério da Saúde do Brasil 2016). Therefore, this study has aimed at correlating the symptoms reported with the findings of neurological assessment in upper and lower limbs of leprosy patients.

## Materials and Methods

This analytical cross-sectional study was conducted at the Ambulatory of the Nucleus of Tropical Medicine of the Federal University of Pará (UFPA), located in Belém, capital of the state of Pará, Brazil. The precepts of human research norms established by Resolution 466/12 of the National Health Council and the recommendations of the research ethics committee for human beings of the Nucleus of Tropical Medicine-UFPA was respected, with approval granted by the opinion nº 1.331.415.

The study included leprosy patients who came to the service for the follow-up of the disease between the years 2014 and 2015, were older than 18 years, of both sexes, diagnosed with leprosy by a dermatologist according to the Madrid classification as Indeterminate Leprosy (IL), Tuberculoid Leprosy (TL), Borderline Leprosy (BL) and Lepromatous Leprosy (LL), as confirmed by skin smear and histopathological tests. Those who had other leprosy-associated diseases such as Acquired Immunodeficiency Syndrome, Diabetes, Human T-lymphotropic Virus (HTLV), rheumatoid arthritis, neurotoxoplasmosis, and previous sensory and / or motor changes other than leprosy were excluded.

For the data collection, all the patients were submitted to the simplified neurological evaluation recommended by the Ministry of Health of Brazil, extracted from the Manual of Prevention of Disabilities (Ministério da Saúde do Brasil 2001). Information was recorded regarding the characteristics of the patient and the disease, degree of disability, symptoms, palpation of the nerves, sensitivity and muscular strength of upper and lower limbs.

Patients were questioned about the occurrence

of the most common symptoms in the disease and the reported symptoms were grouped according to the possible types of nerve fibers involved. In the symptoms related to the sensory fibers were the numbness, tingling, shock and pain, the symptoms related to the motor fibers was considered the muscular weakness. When the patient referred to muscle weakness with one or more sensory symptoms, it was framed in the symptoms related to sensory-motor fibers.

Palpation of the nerve was performed according to the technique described by Lehman et al (1997), in a specific area for each of the nerves most affected in leprosy, being ulnar, medial and radial nerves for upper limbs and common fibular and posterior tibial nerves, for lower limbs. We sought to verify the presence of electric shocks sensations or pain on palpation, and thickening of the nerve.

The sensory testing of hands and feet was done using Semmes Weinstein monofilaments, that is the most common technique and with considerable applicability in pratice, besides being highly reliable and low cost. In order to categorize the data, classification developed by Souza et al (2005) and applied to leprosy by Conceição (2012), which divides the results obtained with the monofilaments into five stages, considering sensitive damage from stage 2. For this research, because it was a hands and feet assessment, a small adaptation was made for the blue monofilament, being considered stage 1 for the feet and stage 2 for the hands, since there is already some damage in the sensitivity of hands, with prejudice to fine discrimination (Table 1).

The technique chosen for the assessment of muscular strength is the voluntary muscle test (VMT), considered standard for motor tests in leprosy (Suresh et al 2009). The categorization of the results considered the numerical scores from zero to five, according to the response presented by the individual.

The statistical analysis was made in the software Bioestat 5.4®. For the comparison between groups, the Chi-square test, G test or t test was used. For the correlation of ordinal variables, the Spearman correlation test was used. The alpha level of significance was considered as 0.05.

**Table 1 : Stages of sensory damage according to the force of the Semmes Weinstein monofilament felt by the leprosy patients.** ***(Conceição (2012), Adapted by the author)***

| Monofilament (Color) | Interpretation | Stage |
|---|---|---|
| 0.05 gf (green) | Normal sensitivity for hands and feet. | 1 |
| 0.2 gf (blue) | Sensitivity decreased in the hands, with difficulty in fine discrimination. | 1 (feet) |
| | Normal sensitivity for feet. | 2 (hands) |
| 2.0 gf (purple) | Protective sensitivity decreased, remaining sufficient to prevent injury. | 2 |
| 4.0 gf (red) | Loss of protective sensitivity. | 3 |
| 10.0 gf (orange) | Loss of protective sensitivity, still feeling deep pressure and pain. | 3 |
| 300.0 gf (magenta) | The sensitivity of deep pressure and pain remains. | 4 |
| Does not feel 300.0 gf | Loss of deep pressure sensitivity, usually not feel pain. | 5 |

## Results

A total of 97 leprosy patients were submitted to simplified neurological evaluation. Of these, 20 (20.6%) did not have any type of symptoms and 77 (79.4%) reported some symptoms in the upper or lower limb, or both. The older patients, the bordeline clinical form, the multibacillary WHO operational classification and higher degrees of disability in the lower limbs correlated maximum with the occurrence of symptoms. The reaction was found in 28.6% (n=22) of patients with symptoms and in 5% (n=1) of patients without symptoms.

Of the 77 patients with symptoms, 15 (19.5%) reported symptoms only on upper limbs, 14 (18.2%) only on lower limbs, and 48 (62.4%) on both limbs. Symptoms in upper and lower limbs were mostly related to sensory fibers, followed by symptoms related to sensory-motor fibers and related to motor fibers. There were no statistically significant differences in reported symptoms between the limbs (Table 2).

In the distribution of the most commonly reported symptoms, it is important to notice that numbness was predominant among symptoms related to sensory fibers, representing 43,1% (n=22) in the upper limb and 54,9% (n=28) in the lower limb. Followed by pain, with 29.4% (n=15) and 27.4% (n=15) in upper and lower limbs, respectively. The numbness was also found with higher frequency among the symptoms related to sensory-motor fibers, occurring in association with muscle weakness.

In the group of patients with symptoms, as expected, 94.8% (n=73) of the patients presented some sensory and/or motor damage. In the patients without symptoms, the majority (65.0%, n=13) presented some segment that was compromised with sensory and/or motor alterations, whereas only 7 (35.0%) presented no damage (Fig. 1).

On the other hand, the occurrences of sensory damage among the patients without symptoms had lower damage stages than those presented by the other patientes. Muscle strength in both limbs was also a factor that was related to the presence of symptom, with a higher frequency of low scores in patientes with symptoms. It is noteworthy that, among the patients without symptoms, motor damage in the lower limb was not observed.

The amount of nerve affected is related to the occurrence of symptoms, both for the upper limb and lower limb, where the patients with symptoms present more nerves affected than others patients (Fig. 2).

**Table 2 : The reported symptoms in upper and lower limbs presented according to the nerve fiber involved**

| Symptoms | Upper Limbs n (%) | Lower limbs n (%) |
|---|---|---|
| Related to Sensory Fibers | 37 (58.7) | 41 (66.1) |
| Related to Motor Fibers | 5 (7.9) | 3 (4.8) |
| Related to Sensory-motor Fibers | 9 (14.3) | 11 (17.7) |
| Others Symptoms | 12 (19.1) | 7 (11.3) |
| **Total** | **63 (100.0)** | **62 (100.0)** |

* G test; [a]Test realised between upper and lower limbs, p=0.5417.

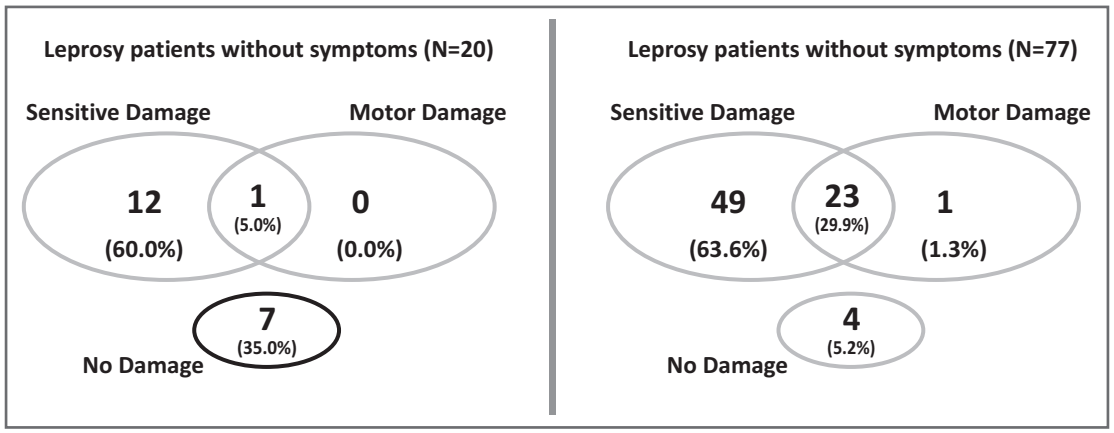


**Fig. 1 : Occurrence of sensory and/or motor damage in patients with or without symptoms**

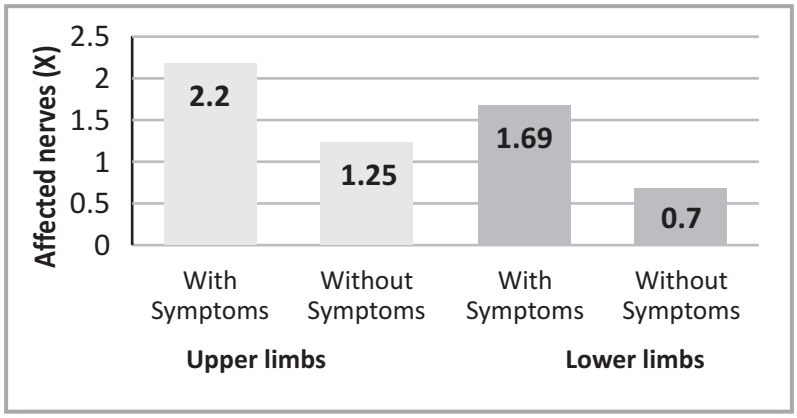


**Fig. 2 : Distribution of patients according to occurrence of complaint and average of affected nerves in upper and lower limbs.**

It was also verified that the variables: sensory damage and number of nerves affected were independent of the type of symptom reported by the patient, if related a sensory, motor or sensory-motor fibers.

Regarding muscle strength, however, there was an association between the type of symptom in the upper limbs, in which patients with sensorial symptoms also had more muscular force involvement.

Correlating the muscle strength with the sensory damage, an inverse proportional relationship was verified for all the movements tested, both upper limb and lower limb, that is, the greater the sensory damage, the lower the muscle strength presented by the patient. The result was significant for almost all movements, the exception was left foot dorsiflexion.

## Discussion

The sensory nerve impairment leads to symptoms such as paresthesia, hypoesthesia and hyper-algesia, although in some cases the change in

sensitivity may develop silently. The motor nerve impairment, in turn, results in decreased strength and loss of associated muscle mass (muscle atrophy) and resulting in deformities (Skacel et al 2000). In this study, most of the leprosy patients presented some type of symptoms, mainly related to sensory fibers, such as: pain, shock, tingling and numbness. The only motor symptoms were the least mentioned, in most cases they appeared together with sensorial alterations.

The occurrence of these symptoms was common during treatment with multidrug therapy, among the older individuals with the most severe form of the disease (multibacillary) and higher degrees of disabilities in the lower limbs. When the symptoms were correlated with the findings of the neurological assessment, it was verified that the patients with symptoms had more advanced sensory damage, a greater frequency of motor damage and a greater number of thickened nerve. The findings are independent of the type of symptoms.

The major involvement of nerves in the multibacillary group is expected. In these cases, in response to bacillary proliferation or rapid changes in cellular immunity and in the presence of reactional episodes, there is rapid formation of granulomas with macrophages, epithelioid and lymphocyte cells, edema and, in some cases, necrotic changes. This leads to a worsening of neurological lesions, which are manifested by symptoms such as: paresthesias, pain and motor and sensory deficits, and reflect in higher degrees of disability (Fleury 1997).

The symptoms which reflect neural involvement usually begin when the nerve has approximately 30% damage to its fibers, so a greater occurrence of sensory and motor changes in patients with symptoms is expected (Pearson & Ross 1975). Véras et al (2012) working with leprosy patients with common fibular nerve lesions, found that individuals with higher pain indexes had lower levels of muscle strength for hallux extension and foot dorsiflexion.

Another study, which aimed at evaluation of patients with symptoms of peripheral neuropathy to confirm or remove the diagnosis of leprosy neuropathy, noticed that the most frequently reported symptoms were hypoaesthesia, paresthesia, neural thickening, nerve pain, paresis and amyotrophy. The sensory damage was found in 100% of the patients with confirmed diagnosis of the disease (Skacel et al 2000).

An unexpected finding in this study was the fact that patients without symptoms also presented with sensory damage, even at lower stages than the patients with symptoms. This disagreement between symptoms and the results of evaluations also occurs occasionally, in sensory neuropathies such as diabetes (Vinik et al 2000, Herman & Kennedy 2005) and carpal tunnel syndrome, one of the explanations would be personal perception or coexistence of other Pathologies that confuse sensory loss (Rumbolt & Hooper 2015).

This may also represent the relative and subjective aspect of the symptoms, in which the psychological state seems to affect the coping of the disease. Correa et al. (2014) verified the frequency of depressive symptoms and their relationship with the degree of disability and socioeconomic variables, and found that the moderate to severe depressive symptom was present in 43.1% of their sample, regardless of whether they had or not disabilities. One of the factors that most influenced depression was occupational impairment, when patients no longer felt useful.

In this study, motor damage was not common among patients. However, when compared with other findings of neurological assessment, such as the sensory damage, it was perceived that it

was directly associated, that is, muscle strength was more affected in individuals with more advanced sensory damage.

Khambati et al (2009) evaluated the sensitivity and specificity of some tests present in the leprosy evaluation and found that the monofilaments and the strength test showed good specificity (<80% and <90%, respectively), but a moderate sensitivity or low, mainly for the test of muscle strength that presented results between 4% and 5%. Kaplan and Gelber (1985), in a similar study, also found that the muscle strength test identifies fewer cases of neuropathies compared to the sensitivity and nerve conduction tests. Various studies, on the other hand, have concluded that, in order to better monitor neural damage, the joint analysis of assessment tests is the best option (Kaplan & Gelber 1985, Garbino & Opromolla 2003, Khambati et al 2009, Dros et al 2009). Khambati et al (2009) observed that monofilaments and the voluntary muscle test combined with palpation of the nerves increased their power to detect nerve involvement, and were comparable to even the nerve conduction test results.

The neurological assessment of leprosy is done by simple tests that are easy to apply and provide useful feedback for patient monitoring; however, many tests depend on the therapist's interpretation. It's necessary taking into account the clinical point of view of the patient and the way he feels the situation for a reliable interpretation of the condition of the leprosy.

## Conclusion

Patients presenting with symptoms of numbness and pain in this study were found to have higher degree of sensory impairment, higher degree of incapacity in lower limbs and occurrence of motor damage more frequently, independent of the type of related symptoms. Sensory damage was also associated with the degree of muscle strength inversely, revealing worse force indices for more severe sensory damage. Thus, it is essential that the health professionals should pay attention not only to the patient's physical changes, but also to the symptoms and complaints. The joint analysis of these aspects will allow a more appropriate evaluation of leprosy patient's condition.

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