Peripheral neuropathy in leprosy: Clinical manifestations and disability in a Colombian national referral center

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Abstract
To aim of the paper was to describe the neurological features of the physical examination in patients with Hansen’s disease who were treated in Bogotá, Colombia. We carried out a descriptive study of all patients with a Hansen’s disease diagnosis treated at a referral center between 2003-2018. There were 327 eligible electronic health records (EHRs) with a final sample of 282 subjects. Leprosy was most common in males (57.45%), median age at the diagnosis was 54 years, and lesions of the lower limbs were more common (75.1%). The median time from disease onset to consult was 12 months. Most of them were classified as having lepromatous leprosy (39.7%). Pain over the median nerve trunk was the most common manifestation of disease (28%), followed by pain over the radial trunk (22%). Sensitive alterations were more common than motor ones. Specifically, the posterior tibial nerve was affected in nearly half of subjects. Dual impairment was more common in the ulnar nerve (13.8%). Some disability was apparent in 23.8% of subjects; predominantly grade 1 disability. Findings regarding age, leprosy type, and the frequency of individual nerve compromise were consistent with reports from other countries. Nerve trunk thickening was infrequent, which might be a consequence of subjectiveness in the examination and sample differences in sex distribution, degree of disability and time since disease onset. The frequency of morbidity and disability found in this sample, though low when compared with other series, fails to meet public health goals, including those limiting disability in younger subjects.

Introduction
In the global update report published by the World Health Organization (WHO) for 2019, a total of 202,185 new cases of Hansen’s disease were reported (25.9 per million inhabitants), of which 10,813 had grade 2 disability.1 This report showed that disease transmission persists and is a public health issue in some countries. Such is the case in Colombia, where detection rates have been reduced only minimally between 2015 and 2019 (0.82 to 0.77 per 100,000 inhabitants).2 In the last 10 years, Colombia has had an average of 400 new cases per year (366 in 2019), of which 7% correspond to children, showing that disease transmission is active.2,3

Detection of neuropathy in its early stages is not straightforward, often requiring significant clinical experience. Neurological alterations become clinically detectable only after fiber destruction has progressed past 30%, and they vary significantly between leprosy types.4–6 Overall, patients with high cellular reactivity (hypohpergia) have a tuberculoid (TL) or borderline tuberculoid (BT) presentation and display faster and greater neuropathic compromise compared to multibacillary forms. The most frequent neurological manifestations are peripheral mononeuropathy (involvement of a single nerve trunk) which occurs mainly in the tuberculoid pole. Asymmetric multiple mononeuropathy (affection of two or more peripheral nerve trunks), appears mainly in dimorphic, lepromatous states and lepromatous reactions. The ulnar, common peroneal, radial, posterior tibial, median and sural nerves are the main nerves involved.7–11

The spectrum of leprosy most associated with physical deformities is borderline leprosy, which leads to abrupt changes in the immune system that lead to a rapid involvement of various nerve trunks. Periodic clinical evaluation is essential in these patients, as well as the assessment of the level of disability at the time of diagnosis, which is carried out based on a standardized classification by the WHO.12

Descriptions of the clinical presentation of neuropathy in leprosy are scarce and often show large variations between countries. No such descriptions are available in our country and neuropathy is often overlooked by clinicians who do not know what manifestations are most common. The aim of this study was to describe the clinical manifestations of neuropathy in patients with Hansen’s disease who were treated at a national referral center for leprosy in Bogotá D.C., Colombia.
between January 2003 and December 2018 in Bogotá D.C., Colombia. We selected EHRs of patients with a diagnosis of leprosy confirmed by a positive bacilloscopic or pathology report. We extracted data on patient demographics, clinical characteristics of the lesions, including location and type, and features of a neurological examination.

We manually analyzed each EHR to determine the validity of the diagnosis. We excluded records with invalid diagnoses and those of patients who had not reported grade of disability. Quality of data input was verified at increments of 15% of the sample initially identified. No pre-specified sample size was defined, and all records were considered for data extraction.

**Study variables**

We extracted data on the dates of onset, diagnosis, sex, place of origin, type of lesion, affected skin areas, and type of leprosy. We also extracted data on the results of an exhaustive neurological examination aimed at the detection of peripheral neuropathy. Disability grades (eye, hand, foot and global) were collected as well. Treatment is reported as multi or paucibacillary. Multibacillary treatment consisted of rifampin, clofazimine and dapsone, while paucibacillary treatment consisted of rifampin and dapsone only.

**Statistical analysis**

We present measures of central tendency and dispersion as appropriate for the underlying distribution of continuous variables. Qualitative variables are presented as absolute and relative frequencies. Type and lesion location frequencies are summarized in UpSet plots. All analyses were carried out using R v.4.0.2.

**Results**

The diagnostic code search produced 327 eligible EHRs. We discarded 45 records due to invalid diagnoses (misdiagnosis), lack of a report of degree of disability, or missing bacilloscopy or pathology results. Subjects were also excluded if they had negative results in both the bacilloscopy and the pathology report. The final sample consisted of 282 subjects, 48 of which had a normal neurological examination.

Our sample consisted of slightly more males than females, with a median age at diagnosis of 54 years. The patients’ place of residence was most commonly urban, though slightly under 19% resided in rural communities, and most were first time con-

![Figure 1. Lesion Characterization A. Type B. Location.](image-url)
ly affected region. The face was the least compromised area with 43.3% of the cases. Most patients presented with lesions distributed over all body regions considered (22.7%), the second most common pattern including all regions but the face (18.09%) (Figure 1B).

Less than 15% of our subjects had a WHO degree of disability (Table 4) of 1 in individual body parts.12 Likewise, less than 10% were graded as 2 in the body parts considered. Manifestations of grade 2 disability included the benediction sign, the absence of the uvula, and finger and nail dystrophy (Figure 2). The eyes were least likely to be compromised. Globally, 23.8% of our patients had some degree of disability.

Discussion

Given the considerable morbidity that

Table 1. Clinical and epidemiologic characteristics of 282 study participants.

| Variable               | N (%) |
|------------------------|-------|
| Male Sex               | 162 (57.45) |
| Marital status         |       |
| Single                 | 143 (50.71) |
| Common-law marriage    | 38 (13.48)  |
| Marriage               | 69 (24.47)  |
| Divorced               | 19 (6.74)   |
| Widowed                | 13 (4.61)   |
| Urban residents        | 229 (81.21) |
| Primary complaint      |       |
| First time consult     | 229 (81.21) |
| Relapse                | 53 (18.79)  |
| Positive Bacilloscopy  | 174 (61.7)  |
| Bacillary Index        |       |
| Negative               | 107 (37.94) |
| Paucibacillary         | 6 (2.13)    |
| Multibacillary         | 160 (59.03) |
| (+) Pathology Report   | 281 (99.65) |
| Leprosy type           |       |
| Tuberculoid            | 20 (7.09)   |
| Borderline tuberculoid | 54 (19.15)  |
| Borderline             | 36 (12.77)  |
| Borderline lepromatous | 47 (16.67)  |
| Lepromatous            | 112 (39.72) |
| Pure neuritic          | 2 (0.71)    |
| Indeterminate          | 11 (3.9)    |
| Lepromatous Reaction   |       |
| Type I                 | 62 (21.99)  |
| Type II                | 26 (9.22)   |
| Both                   | 1 (0.35)    |
| None                   | 193 (68.44) |
| Prior Treatment        |       |
| Multibacillary         | 35 (12.41)  |
| Paucibacillary         | 9 (3.19)    |
| Other                  | 9 (3.19)    |
| No treatment           | 229 (81.21) |
| Age at diagnosis, Median (IQR) | 54 (26) |
| Time since first skin lesion (years) | 1 (2) |

Table 2. Disease manifestations in nerve trunks.

| Nerve/Region          | None | Pain | Thickening | Both |
|-----------------------|------|------|------------|------|
| Auricular             | 272 (96.45) | 2 (0.71) | 2 (0.71) | 6 (2.13) |
| Ulnar                 | 197 (69.86) | 57 (20.21) | 4 (1.42) | 24 (8.51) |
| Median                | 167 (59.22) | 79 (28.01) | 8 (2.64) | 28 (9.93) |
| Radial                | 184 (65.25) | 62 (21.99) | 12 (4.26) | 24 (8.51) |
| Sciatic-popliteal     | 243 (86.17) | 16 (5.67) | 17 (6.03) | 6 (2.13) |
| Posterior tibial      | 246 (87.23) | 13 (4.61) | 14 (4.96) | 9 (3.19) |
| Sural                 | 265 (93.97) | 7 (2.48) | 6 (2.13) | 4 (1.42) |

Table 3. Type of impairment by examined nerve.

| Nerve/Region          | None | Type of impairment |
|-----------------------|------|--------------------|
|                        |      | Sensitive | Motor | Both |
| Face (Trigeminal/Facial) | 237 (84.04) | 29 (10.28) | 3 (4.61) | 1 (0.66) |
| Radial                | 198 (70.21) | 65 (23.05) | 4 (1.42) | 15 (5.32) |
| Median                | 155 (54.96) | 71 (25.18) | 17 (6.03) | 39 (13.83) |
| Ulnar                 | 195 (69.15) | 60 (21.28) | 15 (5.32) | 12 (4.26) |
| Anterior tibial       | 183 (64.89) | 73 (25.89) | 6 (2.13) | 20 (7.09) |
| Posterior tibial      | 134 (47.52) | 129 (45.74) | 1 (0.35) | 18 (6.38) |

Table 4. Degree of disability.

| Body Part | 0 | 1 | 2 |
|-----------|---|---|---|
| Right Hand| 257 (91.13) | 14 (4.96) | 11 (3.8) |
| Left Hand | 253 (89.72) | 11 (3.9) | 18 (6.38) |
| Right Foot| 236 (83.89) | 34 (12.06) | 12 (4.26) |
| Left Foot | 233 (82.62) | 42 (14.89) | 7 (2.48) |
| Right Eye | 275 (97.52) | 4 (1.42) | 3 (1.06) |
| Left Eye  | 275 (97.52) | 2 (0.71) | 5 (1.77) |
| Global Disability| 215 (76.24) | 35 (12.41) | 32 (11.35) |

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variable incubation times. Two subjects below the age of 15 were identified in this study, one of whom displayed grade 2 disability. Different public policies on leprosy eradication, both global and national, have key goals of no new cases in children and no cases with visible deformity, so these two cases point to deficiencies in our public health system.

Most of our patients had a diagnosis of multibacillary leprosy or borderline forms, both of which are more prone to neuropathic manifestations, as shown by Moschioni et al. Leprotic reactions are key risk factors which increase risk by up to 96% (type I most common in our study). Other key factors are the involvement of three or more nerve trunks, greater time since disease onset (>1 year) and multibacillary states. This would explain the disability distribution in our patients, most of whom were diagnosed after at least one year from symptom onset. In other reports, 27.7% of patients had grade 1 disability and 12.1% to grade 2.

Other retrospective observational studies have shown that neuropathy may arise at any moment, regardless of treatment. Although early treatment reduces the frequency of neuropathy in groups of patients, this does not mean that vigilance must be relaxed over time in individual patients. Remaining vigilant may help prevent severe complications. For example, our study showed that the anterior and posterior tibial nerves were most commonly affected, the latter being a risk factor for complications related to plantar anesthesia like ulcers, deformity and even bone resorption.

Unlike previous reports, neural thickening was not a frequent finding in our population. Between 75-94% of cases in a cohort of 303 patients with lepromatous leprosy displayed this alteration in a multi-center study carried out in India. However, that cohort differed significantly from our sample with regards to reported risk factors for nerve thickening. The Indian cohort included significantly more males (72.6%), had patients with greater times since disease onset (38.2% over 12 months), and a greater degree of disability (50.5%). Variations in the frequency of this finding may also be explained by the subjectiveness of the examination, in which the physician palpates the compromised nerve trunks. It has been shown that agreement between physical examination by experienced personnel and nerve ultrasonography is of only 0.3. Imaging has the advantage of being able to evaluate a greater portion of the nerve, including portions that lie deep to the skin, where palpation cannot identify any changes. Although the clinical utility of ultrasonography in the management of leprosy is yet to be shown, it appears that efforts to educate physicians in nerve palpation may be fruitless.

The evaluation of the degree of disability was one of the key objectives for this study since this represents an early diagnostic marker of leprosy. Early detection of peripheral neuropathy is complex, mainly because it is highly dependent on the physician’s experience. In the early stages of the disease itself, clinical manifestations of neural impairment might be imperceptible. Both the clinical examination and the interpretation of diagnostic testing depend on clinical expertise to make them reliable. Additionally, healthcare workers in Colombia show a lack of knowledge of this disease. This was shown by Gómez et al. in a study on 249 patients, up to 70% of which had initially been misdiagnosed and mistreated. That study also found that the average delay from disease onset to diagnosis was of 33.5 months, and that 14.5% of the subjects had grade 2 disability at diagnosis. This might account for the high frequency of neurological alterations and disability in the Colombian population.

**Conclusions**

In this study, the age and leprosy type distributions in patients with neuropathy were consistent with reports from other countries. The anterior tibial, ulnar and posterior tibial nerves were most commonly affected which is also consistent with prior reports. However, nerve trunk thickening was much more infrequent, which might be a consequence of subjectiveness in the examination and differences in sex distributions.
tion, degree of disability and time since disease onset. The frequency of morbidity and disability found in this sample, though low when compared with other series, fails to meet public health goals, including those limiting disability in younger subjects.

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