Prevalence and characteristics of neuropathic pain in leprosy patients treated years ago

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The aim of this study was to determine the prevalence of neuropathic pain, now recognized as another late complication of leprosy, and its characteristics among leprosy patients. A cross-sectional study was carried out of people treated for leprosy up to at least 5 years ago in a rural area of Ethiopia. Seventy-four patients were interviewed using the Neuropathic Pain Symptom Inventory (NPSI) questionnaire. In total, 78.9% of the patients were female with a mean age of 42.9. The mean time from initial diagnosis to the time of the study was 28.0 years, and 73.0% of patients were diagnosed over 20 years ago. Fifty-two (70.3%) reported having symptoms suggestive of neuropathic pain and the majority described the pain as burning (88.5%), electric (80.8%), stabbing (76.9%), cutting (76.9%), tingling (65.4%), squeezing (57.7%), and/or pressure (53.8%). The pain caused a severe or moderate impact on daily life in 75% and 57.7% of cases, respectively, and 92.3% suffered from disrupted sleep. Eighty percent of patients with pain (42/52) took some medication for pain relief. Neuropathic pain is common in patients treated for leprosy and in more than half of them, it causes disruption in their daily life and sleep, limiting their quality of life even more.

Keywords: Neuropathic pain, Leprosy, Quality of life, Ethiopia

Background

Leprosy is a chronic disease with low-grade infectivity caused by *Mycobacterium leprae*, affecting the peripheral nerves, skin, and certain body tissues, which can lead to deformities, physical disability and social stigma.[1] The number of leprosy cases registered worldwide decreased from 5 351 408 in 1985 to 926 259 in 1996, and in 2012, 181 941 cases were registered.[2–4] Leprosy causes some degree of peripheral nerve damage in a high percentage of cases, and pain can occur when there is an acute inflammation in one or more nerves associated with reactions. After appropriate treatment with steroid and anti-inflammatory medications, the pain can subside. However, after successful treatment with multidrug therapy, some patients may suffer from chronic pain, termed as neuropathic pain.[5]

Neuropathic pain occurs as a direct consequence of a lesion or disease affecting the somatosensory system.[5] It can be so severe that it significantly impairs the patient's quality of life,[6] and moreover, it does not respond to the usual analgesics used for reactions.[5,6] So far, little attention has been paid to this problem in leprosy patients. In 2000, Hietaharju *et al.*[7] described the clinical findings of 16 Bangladeshi patients with multibacillary leprosy who had chronic stimulus-independent pain despite finishing their treatment. There are several reports about neuropathic pain in people treated for leprosy and most of them have appeared as recently as the twenty-first century.[7–11]

The epidemiological profile of neuropathic pain in patients with leprosy has been described, but the study of the risk factors of developing neuropathic pain is scant.[10,11] The aim of this study was to determine the prevalence of neuropathic pain and its characteristics among leprosy patients from southern Ethiopia who had finished their treatment at least 5 years before.

Patients and Methods

This is a non-institution-based cross-sectional survey, which was conducted during February and March 2013 in a village near Gambo Rural General Hospital, in the West Arsi zone and 250 km south of Addis Ababa. The hospital is a rural referral institution for Ethiopia's leprosy care program according to the

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Ministry of Health guidelines for the Tuberculosis and Leprosy Prevention and Control Program (TLPCP).[12] The original Leprosy Centre was built in Gambo in 1960, and it supervised 20 leprosy care stations in the Arsi Region. It worked in this way until 1986 when it became a General Hospital. During this period, some leprosy patients built houses around the hospital and started living there.

First, the researchers explained the purpose of the study to patients and asked them for their spoken consent to be interviewed. Patients were then interviewed in a meeting room and an examination room by a doctor and a healthcare assistant using the Neuropathic Pain Symptom Inventory (NPSI) questionnaire, The questionnaire included the following variables: date, name, gender, town, time since diagnosis of leprosy (years), type of leprosy (paucibacillary or multibacillary), antecedent of leprosy reaction, type of treatment (MDT multidrug therapy or dapsone), and treatment with steroids at any time. Each leprosy case was assessed for disability and assigned a disability grade for each eye, hand and foot, which showed the condition of the patient at diagnosis. The WHO disability grading is 0, 1, or 2, and disabilities were graded according to the TLPCP.[12]

Once the NPSI questionnaire was administered,[13] the intensity of pain was measured on an 11-point Likert continuum (the left end was labeled as no pain and the right end as the worst pain imaginable),[13,14] and a verbal rating scale (mild, moderate, and severe). The location of pain was recorded by using pain drawings:[14] pain in glove-like distribution and pain in stocking-like distribution.

Patients were also asked about the nature of the pain, which was then recorded In order to distinguish nociceptive pain caused by neuritis/reactions from neuropathic pain, we defined neuropathic pain following the criteria by Chen *et al.*:[11] a pain condition which occurred after at least 2 years of anti-leprosy treatment and lasted for at least 3 months (continuous or interrupted) without any evidence suggestive of reactions and other causes, such as infected ulcers. Other potential causes of neuropathic pain were assessed through clinical history and physical examination, and patients with other conditions causing neuropathic pain, such as diabetes, alcoholic polyneuropathy, or depression, were excluded.

Data were entered in an Excel 97 database, and the statistical analysis was made using SPSS software, version 21. Continuous variables are given as mean and standard deviation (SD). A Student's *t*-test was applied for continuous data, and a Chi-square test was used for comparison between two or three categorical variables. Fisher's exact test was used where the sample size of patients was not large enough, and the Kruskal–Wallis test, a non-parametric test, was used to compare the significance of the difference between the distributions of two independent samples.

Ethics approval was obtained from the local Research and Publication Committee of the Gambo Rural General Hospital and the Health Unit and Ethical Review Committee of the Ethiopian Catholic Secretary.

Results

A total of 77 patients with leprosy were interviewed and three patients were excluded, two of which were diabetics and one had a psychiatric disorder. In total, 78.9% ($n=51$) of the 74 patients were females and 31.1% ($n=23$) males. Age ranged from 17 to 89 (mean: 42.9, SD: 12.0) years. The mean time since initial diagnosis of leprosy was 28.0 (range: 5–56; SD: 10.5) years, and 60 (73.0%) patients were diagnosed over 20 years ago. Most patients had MB leprosy (95.9%), and WHO grade 2 disabilities were present in 65 (87.8%) of the patients. Two patients had an amputation on one leg. Combined motor and sensory test results showed that: 67 patients had tibial nerve impairment (90.5%); 60 patients (81.1%) had ulnar nerve impairment; and 40 patients (54.1%) had median nerve impairment.

Fifty-two of the 74 patients (70.3%) had neuropathic pain. Table 1 shows the epidemiological and clinical characteristics of patients with or without neuropathic pain. WHO grade 2 disabilities were more common in patients with neuropathic pain (92.3%) than in patients without neuropathic pain (77.3%) ($P=0.07$). Right tibial nerve lesion was significantly more common in leprosy patients with neuropathic pain than in those without pain (90.4% versus 68.2%; $P=0.02$). Ulnar nerve damage was more common in patients with pain (86.5% versus 68.2%; $P=0.06$). There was no significant difference in the frequency of neuropathic pain in relation to gender, age, type of leprosy, total number of disabilities, and type of treatment used (Table 1).

Eight (15.4%) of these 52 patients had pain in stocking distribution and 7 (13.5%) in glove distribution. The majority described pain as burning (88.5%), electric (80.8%), stabbing (76.9%), cutting (76.9%), tingling (65.4%), squeezing (57.7%), or pressure (53.8%). In total, 73.1% stated that they experienced touch-evoked pain and that the pain was provoked or increased by skin contact (Table 2).

The pain caused a severe and moderate impact on daily life in 75% and 57.7% of cases, respectively, and 92.3% suffered disrupted sleep due to pain. The average score for burning pain was 6.5, for pressing pain 3.6, for paroxysmal pain 5.5, for evoked pain 4.4, and for paresthesia/dysestesia 5.1. Forty-two of the 52 patients with pain (80.7%) took some medication for pain relief, and surprisingly, 75% of them reported that the treatment was effective. The type of pain medication used

Table 1 Patient characteristics of 74 people treated for leprosy, examined according to presence or absence of pain

	Total (*N*=74)	Patients with pain (*N*=52)	Patients without pain (*N*=22)	*P*-value
Age, years (mean, SD)	42.9, 12.0	43.1, 11.4	42.5, 13.6	0.9
Sex, *N* (%)				0.1
Female	51 (68.9)	33 (65.5)	18 (81.8)	
Male	23 (31.1)	19 (36.5)	4 (18.2)	
Education level				0.7
No studies	36 (48.6)	24 (46.2)	12 (54.5)	
Basic (grade 1–4)	27 (36.5)	20 (38.5)	7 (31.8)	
Elemental (grade 5–8)	11 (14.9)	8 (15.4)	3 (13.6)	
Years since leprosy diagnosis (mean, SD)	28.0, 10.5	28.6, 10.3	26.8, 11.2	0.5
Type of leprosy, *N* (%)				0.9
MB	71 (95.9)	50 (96.2)	22 (95.7)	
PB	3 (4.1)	2 (3.8)	1 (4.3)	
Type of treatment, *N* (%)				1
MDT	36 (48.6)	26 (50)	11 (50)	
DDS	38 (51.4)	26 (50	11 (50)	
WHO grade 2 disability, *N* (%)				0.07
Yes	65 (87.8)	48 (92.3)	17 (77.3)	
No	9 (12.2)	4 (7.7)	5 (22.7)	
Total disabilities (mean, SD)	6.7, 12.9	6.9, 2.6	6.3, 3.8	0.4
Treatment with steroids at any time, *N* (%)				0.17
Yes	39 (52.7)	29 (55.8)	10 (45.5	
No	29 (39.2)	17 (32.7)	12 (54.5)	
Unknown	6 (8.1)	6 (11.5)	0	
Number of nerves affected (mean, SD)	4.4, 2.2	4.6, 2.1	3.9, 2.3	0.2
Ulnar nerve, *N* (%)	60 (81.1)	45 (86.5)	15 (68.2)	0.06
Right, *N* (%)	56 (75.7)	40 (76.9)	16 (72.7)	0.08
Left, *N* (%)	51 (68.9)	39 (75.0)	12 (54.5)	0.7
Medial nerve, *N* (%)	40 (54.1)	28 (53.8)	12 (54.5)	0.9
Right, *N* (%)	37 (50)	26 (50)	11 (50)	1
Left, *N* (%)	32 (43.2)	22 (42.3)	10 (45.5)	0.8
Tibial nerve, *N* (%)	67 (90.5)	49 (94.2)	18 (81.8)	0.09
Right, *N* (%)	62 (83.8)	47 (90.4)	15 (68.2)	0.02
Left, *N* (%)	12 (16.2)	45 (86.5)	17 (73.0)	0.3
Peroneal nerve, *N* (%)	23 (31.1)	18 (34.6)	5 (22.7)	0.3
Right, *N* (%)	21 (28.4)	16 (30.1)	5 (22.5)	0.5
Left, *N* (%)	19 (25.7)	15 (30.1)	4 (18.29	0.3

Note: SD: standard deviation; MB: multibacillary leprosy; PB: paucibacillary leprosy; MDT: multidrug therapy; DDS: dapsone.

was: paracetamol (n=35; 67.3%) or non-steroid anti-inflammatory (n=3; 4.2%) and an unknown type of medication (n=14; 26.9%).

Thirty-six of the 52 patients with neuropathic pain (65.4%) did not relate it to leprosy, and 18 (34.6%) did. Pain provoked or increased by brushing on the painful area was more common in patients with pain attributed to leprosy (81.3%) than in other patients whose pain was attributed to other causes (47.3%, P=0.02). The average score for evoked pain was 5.0 versus 4.2.

Discussion

Neuropathic pain is now recognized as another late complication for leprosy patients.[5,6,15] Our study shows that 70.3% of people affected by leprosy have symptoms suggestive of neuropathic pain. This prevalence is higher than the data reported in previous studies about neuropathic pain in people affected by leprosy (Table 3).[8–11,16] One reason for this is clearly the target population, which has a mean age of about 43 years, and a high disability (grade 2 disability in 87.8% of the patients), which is to be expected due to the long period of time since initial diagnosis (mean: 28.0 years). Another reason might be due to the use of different questionnaires for the study of neuropathic pain and the different characteristics of patients affected by leprosy in the studies.

The main problem is that the scale for measuring neuropathic pain has not been properly validated and different authors have used different scales to measure pain. We used the NPSI questionnaire, but other authors have used other questionnaires, such as an abbreviated version of NPSI, the McGill Pain questionnaire, Douleur Neuropathique in 4 Questions (DN4) or the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS).[8–11,16]

The NPSI has recently been developed and validated,[13,17] and it has been used in several studies on people affected by leprosy.[9,11] It allows discrimination and quantification of the distinct and clinically relevant dimensions of neuropathic pain syndromes (spontaneous ongoing pain, spontaneous paroxysmal pain, evoked pain, and paresthesia/dysesthesia) that are sensitive to treatment.[13,17] The DN4 is another questionnaire, which might be a simple tool for the screening of neuropathic pain in leprosy patients.[10]

In our study, the analysis of the risk factors of neuropathic pain in people treated for leprosy show that only the presence of leprosy-related impairments

Table 2 Characteristics of the pain

	Total patients with pain (*N*=52)
Burning pain	
N (%)	46 (88.5)
Mean, SD	6.5, 3.5
Squeezing pain	
N (%)	30 (57.7)
Mean, SD	3.8, 3.8
Pressure pain	
N (%)	28 (53.8)
Mean, SD	3.6, 3.8
Duration spontaneous pain in 24 hours, *N* (%)	
Permanently	27 (55.6)
4–12 hours	4 (7.7)
<3 hours	21 (40.4)
Electric pain	
N (%)	42 (80.8)
Mean, SD	5.9, 4.5
Stabbing pain	
N (%)	40 (76.9)
Mean, SD	5.2, 3.5
Number of attacks during the last 24 hours, *N* (%)	
>6	11 (21.2)
1–5	4 (7.7)
No pain attack	37 (71.2)
Pain provoked or increased by brushing on the painful area	
N (%)	30 (57.7)
Mean, SD	4.2, 4.1
Pain provoked or increased by pressure on the painful area	
N (%)	37 (71.2)
Mean, SD	4.8, 3.8
Pain provoked or increased by contact on the painful area	
N (%)	38 (73.1)
Mean, SD	4.5, 3.5
Pricking pain	
N (%)	40 (76.9)
Mean, SD	5.8, 3.6
Tingling pain	
N (%)	34 (65.4)
Mean, SD	4.5, 3.9
Impact on daily life, *N* (%)	
Mild	9 (17.3)
Moderate	30 (57.7)
Severe	13 (25)
Sleep disruption, *N* (%)	
Yes	48 (92.3)
No	4 (7.7)
Pain stops sleep, *N* (%)	
Mild	20 (38.5)
Moderate	25 (48.1)
Severe	7 (13.5)

(nerve enrollment and disability grade 2) is a slightly significant factor. This is also evident in other studies: Saunderson *et al.*[9] found that impairment at diagnosis was a risk factor of neuropathic pain; Larsy-Levy *et al.*[11] showed that nerve enlargement, nerve tenderness, trigeminal nerve impairment, and painful skin

Table 3 Prevalence of neuropathic pain in leprosy patients

	Number of patients studied	Country	Type of patients	Questionnaires administrated	Prevalence neuropathic pain
This study	74	Ethiopia	Treated of leprosy	NPSI	70.3%
Strump *et al.* (2004)[8]	358	Brazil	Treated of leprosy	McGill Pain Questionnaire	56%
Chen *et al.* (2012)[11]	275	China	Treated of leprosy	NPS	45.8%
Saunderson *et al.* (2008)[9]	96	Ethiopia	Treated of leprosy	NPSI	29%
Lasry-Levy *et al.* (2011)[10]	101	India	Treated of leprosy	DN4	21.8%
Haroun *et al.* (2012)[16]	80	Ethiopia	Recently treated leprosy patients	DN4 and LANSS	17%

Note: DN4: Douleur Neuropathique en 4 Questions (DN4); LANSS: Leeds Assessment of Neuropathic Symptoms and Signs; NPSI: Neuropathic Pain Symptom Inventory.

patches were associated with neuropathic pain; and Chen *et al.*'s[10] analysis, using a multivariable model for the development of neuropathic pain, showed that a previous history of type-2 reaction had a significant association with neuropathic pain.

A previous study by Lund *et al.* in 17 patients showed evidence of ongoing intraneural inflammation and perineural thickening in leprosy patients who had completed treatment and had chronic neuropathic pain.[18] By using intraepidermal nerve density measurements, these patients were shown to have small-fiber neuropathy.[18]

The management of patients with established neuropathic pain may require healthcare services for many years[5,6,16] and a high intake of analgesics.[19] However, neuropathic pain does not respond to the usual analgesics used for reactions[5,15] and in our study, the most commonly used anti-pain treatment was paracetamol, because it is a cheap and available drug. Other effective drugs for neuropathic pain are tricyclic antidepressants and anticonvulsant drugs, which would be cost-effective in developing countries,[7] but are rarely used. Modern pain-killers are expensive and not easy to find in the rural areas of low-income countries, in which case more research is required to define the anti-pain regimes to be used and define appropriate alternatives for neuropathic pain in previously treated leprosy patients in these countries.

Neuropathic pain is associated with psychological morbidity and quality of life comorbidities.[20] Leprosy and neuropathic pain may have separate and perhaps synergistic contributions to psychological morbidity.[19] Recently, Lasry-Levi *et al.*[10] and Haroun *et al.*[16] have used the 12-item General Health Questionnaire to identify neuropathic pain and psychological morbidity in patients affected with leprosy. They detected that about 40% of the patients with neuropathic pain had psychological morbidity.[10,16] In our study, we have not measured psychological morbidity by means of a specific questionnaire. However, we have found limitations in the quality of life of the patients with chronic pain and sleeping disorders, as shown in other studies.[9,11]

Neuropathic pain is a forgotten problem in leprosy patients. Its high prevalence is not negligible and it is associated with a low quality of life.

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Conflicts of interest None.

Ethics approval Ethics approval was obtained from the local Research and Publication Committee of the Gambo Rural General Hospital and the Health Unit and Ethical Review Committee of the Ethiopian Catholic Secretary.

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