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Original Article

Clinico-sociodemographic profile of leprosy neuropathy in Medan, Indonesia

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Abstract

Background Leprosy neuropathy is still a serious health issue in emerging and underdeveloped nations. Nerve damage caused by leprosy that is not handled properly and quickly will cause disability. Therefore, information about characteristic of leprosy patients with neuropathy is very necessary. The purpose of this study is to identify the clinico-sociodemographic characteristics of leprosy patients who have neuropathy.

Methods This is a cross-sectional descriptive study that uses the consecutive sampling strategy on 21 leprosy patients who have neuropathy. Leprosy neuropathy was examined using Semmes-Weinstein monofilaments.

Results Sociodemographic characteristics were mostly in the age group 18-35 years (57.1%), male (85.7%), secondary education level (57.1%), and work as employee (33.3%). The majority of the research subjects were multibacillary (MB) type leprosy (100%), experiencing leprosy reactions (42.9%), release from treatment (RFT) (47.6%), leprosy duration >12 months (57.1%), experienced symptoms of neuropathy (95.2 %), duration of neuropathy symptoms ≤ 1 year (52.4%), neuropathy location in the lower bilateral extremities (52.4%), and did not have a grade 2 leprosy disability according to WHO (90.5%).

Conclusion The majority of leprosy neuropathy patients were in the age group of 18-35 years, male, secondary education level, employee, MB type leprosy, experiencing leprosy reactions, RFT, duration of leprosy >12 months, experienced symptoms of neuropathy, duration of neuropathy symptoms ≤1 year, neuropathy location in the lower bilateral extremities, and did not have a grade 2 leprosy disability according to WHO.

Key words
Disability, leprosy, neuropathy, profile, Semmes-Weinstein monofilaments.

Introduction

A persistent peripheral neuropathy brought on by Mycobacterium leprae is known as leprosy neuropathy. Leprosy neuropathy causes peripheral nerve function abnormalities, including sensory, motor, and autonomic deficits, as well as nerve destruction.[1,2] There was an increase in the leprosy disability rate in Indonesia in 2017 of 6.6/1.000.000 population.[3] In 2016, the frequency of leprosy was 0.1/10.000 people in Medan, Indonesia, while the rate of grade 2 leprosy disability was 0.09/100.000 people.[4] Disability results from nerve damage that is not treated appropriately and promptly so that early diagnosis of leprosy neuropathy can reduce the number of leprosy disabilities.[1,5,6] Leprosy patients who experience physical disabilities are subjected to social stigma and prejudice by the neighborhood

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community, tend to live alone, and the opportunity to earn a living is reduced that cause decrement in quality of life.[7,8]

If there is a disturbance of sensory nerve function, there will be a sensation of numbness in the palms of the hands and feet so that injury can occur easily. Nerve conduction investigations can show functional abnormalities of the nerves in leprosy before the clinical symptoms and signs of the disease manifest. The absence of clinically detectable neurological dysfunction may be a preclinical stage of damage. Symptoms of neuropathy can include pain, heat, numbness, tingling or prickling. When clinical symptoms are clearly felt, certain nerve fibers become dysfunctional. Thirty percent of sensory nerve fibers need to be affected by leprosy bacilli before sensory deficits become clinically apparent. Sensory nerve damage occurs early and most frequently in leprosy.[9,10]

It is challenging to make an early diagnosis of nerve injury with a clinical examination. Nerve damage in the leprosy patient can be identified with additional testing using the Semmes-Weinstein Monofilament (SMW) test.[1,5] Since there are few studies on the characteristics of leprosy neuropathy patients, the goal of this study is to gather fundamental information for future studies on leprosy neuropathy, including clinico-sociodemographic information of leprosy patients with neuropathy.

Methods

This is a cross-sectional descriptive study that used the consecutive sampling procedure on 21 leprosy patients with neuropathy who visited the Universitas Sumatera Utara Hospital, dr. Pirngadi Hospital, and H. Adam Malik Hospital between January to July 2021.

Leprosy patients with neuropathy, aged 18 years or older, and willing to participate in the study by signing informed consent, met the inclusion criteria for this study. Patients with stroke, limb amputation, diabetes mellitus, hypothyroidism, alcoholism, vitamin B12 deficiency, HIV, chemotherapy, consuming colchicine, stavudine, phenytoin, and isoniazid ethambutol, metronidazole, and amiodarone within 6 months were excluded from the study.

Leprosy neuropathy examination was carried out with Semmes-Weinstein monofilament applied to the hands (seven areas) and feet (eight areas) until they were bent in a "C" curve for 1.5 seconds, then slowly released and repeated three times in the same area. The examination begins with the thinnest monofilament (green). If the patient cannot feel the monofilaments, continue with thicker monofilaments. The examination was declared correct if the patient could point within 2 cm from the stimulated area at least twice. Normal sensory threshold reference values with the hand SWM test were 0.2 gm (blue) and 2 gm (purple). The diagnosis of neuropathy can be made when the monofilament threshold increases >3 level at one site or the monofilament threshold increases by 2 levels at one site and increases by one level at the other site or when the monofilament threshold increases by 1 level at 3 sites. The participants underwent a single clinical assessment appointment during which the investigator took a thorough medical history of them, noting their sociodemographic data (age, gender, education and occupation), type of leprosy, history of leprosy reactions, treatment status, and duration of leprosy. Participants were assessed about the presence of neuropathic symptoms, duration of neuropathy symptoms, location of neuropathy and presence of grade 2 leprosy disability.

Descriptive analysis was used to assess the frequency and proportion of each clinical and

sociodemographic characteristic among leprosy patients with neuropathy.

The Faculty of Medicine of the University of Sumatera Utara in Medan's Research Ethics Committee gave its approval to this study.

Results

The sociodemographic characteristics of leprosy patient with neuropathy were shown in **Table 1**. The majority of sociodemographic characteristics were found in the age range 18-68 years and mostly in the group of 18-35 years (57.1%), male (85.7%), secondary education level (57.1%), and work as employee (33.3%).

Table 2 shows the clinical characteristics of leprosy neuropathy. Based on the type of leprosy according to the WHO classification, all of research subjects were MB type leprosy (100%). The distribution of leprosy neuropathy based on a history of leprosy reactions was found that the majority of research subjects were experiencing leprosy reactions (42.9%). Based on leprosy treatment status, the majority of research subjects had RFT (47.6%). Based on the duration of leprosy, the majority of research subjects with leprosy >12 months (57.1%). In this study, subjects were asked about the presence of neuropathy symptoms such as complaints of pain, heat, numbness, tingling or prickling and the majority of research subjects had experienced symptoms of neuropathy (95.2%). The distribution of leprosy neuropathy based on the duration of neuropathy symptoms is shown the majority of research subjects had neuropathy symptoms ≤1 year (52.4%). Leprosy neuropathy examination was performed with Semmes-Weinstein monofilament applied to the hands and feet and the result shows that the majority of neuropathy locations were lower bilateral extremities (52.4%). The majority of

Table 1 Sociodemographic characteristics of research subjects.

Sociodemographic Characteristics	*Frequency (n=21)*	
	N	*%*
Age (Years)		
18 - 35	12	57.1
36 - 55	6	28.6
56 - 75	3	14.3
Gender		
Male	18	85.7
Female	3	14.3
Level of education		
Primary	4	19
Secondary	12	57.1
High	5	23.8
Occupation		
Not Working	6	28.6
Employee	7	33.3
Private Employee	4	19.1
Student	4	19.1

Table 2 Clinical characteristics of leprosy neuropathy.

Clinical Characteristics	*Frequency (n=21)*	
	N	*%*
Leprosy Type		
Paucibacillary (PB)	0	0
Multibacillary (MB)	21	100
Leprosy Reactions		
Never had a leprosy reaction	4	19.0
Having a leprosy reaction	9	42.9
Ever had a leprosy reaction	8	38.1
Treatment Status		
No treatment yet	4	19,0
Under treatment	7	33,3
RFT	10	47,6
Duration of leprosy		
1-6 months	7	33.3
>6-12 months	2	9.5
>12 months	12	57.1
Symptoms of Neuropathy		
No symptoms	1	4.8
With symptoms	20	95.2
Duration of neuropathy symptoms		
>1 year	10	47.6
≤1 year	11	52.4
Location of neuropathy		
Upper unilateral extremity	0	0
Upper bilateral extremities	0	0
Lower unilateral extremity	6	28.6
Lower bilateral extremities	11	52.4
Whole Extremities	4	4
Grade 2 leprosy disability		
Found	19	90.5
Not found	2	9.5

research subjects did not have a grade 2 leprosy disability according to WHO (90.5%).

Discussion

The majority of sociodemographic characteristics were found in the age range 18-68 years and mostly in the group of 18-35 years, male (85.7%), secondary education level (57.1%), and work as employee (33.3%). This is consistent with a study on leprosy neuropathy from Freitas *et al.* which found that age range of the research subjects was 21-80 years and the majority were male (82.4%).[11] Garbino *et al.* reported that the majority of research subjects were male (80.9%) in the age range of 21-60 years.[12] Faridi *et al.* reported that the majority of the research subjects had a high education level (53.3%) and most of them worked as private employee (53.3%).[13]

All subjects in this study were MB type leprosy (100%). Faridi *et al.* also reported that there was a majority of MB type leprosy in their study (70%).[13] Granulomas that form on nerve tissue are identical to the inflammatory reaction in leprosy skin lesions. The formation of granulomas in the nervous tissue is found in all spectrums of leprosy. At the lepromatous pole (LL), the granulomas formed are typically of the macrophage type, whereas tuberculoid leprosy is characterized by a delayed type of hypersensitivity reaction so that the predominance of epithelioid cells is found. In LL, there is extensive segmental demyelination, Wallerian and axonal degeneration may be insidious. In addition, concurrently, regeneration of Schwann cells and small nerve fibers also occurs in areas of fibrosis. Over time, severe endoneural fibrosis results in permanent damage to nerve function. Vascular changes in the nerves are found early in LL patients, including the formation of fenestrations (gaps) between endothelial cells and capillaries, thickening of the basement membrane and sometimes, rarely, progress to end arteritis with partial or complete occlusion of the capillaries. Prospective study of acute nerve damage in leprosy patients in Bangladesh (BANDS) showed greater prevalence of MB (15.32%).[14]

The majorities of research subjects were experiencing leprosy reactions (42.9%) and had experienced leprosy reactions (38.1%). The incidence of nerve damage in leprosy reactions has been widely known, but what triggers the reaction is still uncertain. In the type 1 leprosy reaction, the neuritis that occurs is the result of increased inflammatory activity from the delayed type hypersensitivity reaction (cellular immunity) in response to mycobacterium antigens. Edema that occurs during the reaction increases the pressure within the larger nerve causing demyelination, axonal damage, and impaired nerve conduction. In type 2 leprosy reaction (ENL), the inflammatory response is caused by antigen-antibody complexes that circulate and spread to several body tissues including nerves. The alternative complement pathway is first directly activated during the early stages of inflammation by M. leprae breakdown products and immune complexes that have been deposited.[15] This activation causes migration of polymorphonuclear neutrophils (PMNs) to nerves, resulting in increased edema and inflammation leading to more severe nerve damage.[1]

Most of the participants in this study had RFT (47.6%). Neuropathy is recognized not only in patients with active disease but also in those who have completed MDT treatment, and can be a major complaint in patients released from treatment (RFT) and last from months to years. This condition includes a broad spectrum of symptoms such as paresthesias, dysesthesias, hyperesthesias, and allodynia along the nerves and areas of distribution. The incidence of

paresthesia was found to be around 24% in a study in India.[16] Rathod *et al*. found that 21.25 percent of disabilities in patients with RFT who were detected during the follow-up period happened as a result of continued nerve damage even after leprosy therapy was finished. Both the establishment of clinical and serological signs indicative of nerve injury and the identification of treatment outcomes are urgently required. Nerve injury is associated with secondary disabilities.[17]

In this study, the majority of research subjects had experienced clinical symptoms of neuropathy, with duration of neuropathic symptoms 1 year and leprosy duration >12 months. Leprosy neuropathy commonly manifests as numbness, anhidrosis, painless ulcers, anesthesia, hyposthesia, and patchy motor deficits. Positivity in the senses including paraesthesias, aches (allodynia and dysaesthesias), and hyperhidrosis are less frequent but frequently indicate the beginning of a leprosy reaction.[18] Detection of sensory disturbances from monofilament is not always followed by subjective complaints, vice versa. However, for a subclinical neuropathy in a close contact due to a humoral immune reaction, subjective neuropathy complaints will arise in the advanced phase, not in the early phase.[19] When clinical symptoms are clearly felt, certain nerve fibers become dysfunctional.[9,10]

In this study, the majority of neuropathy location was in the lower bilateral extremities (52.4%). Rathod *et al.* reported that neuropathy was most common in the upper bilateral extremities (60.5%) and lower bilateral extremities (60.52%).[17] It is generally observed that the nerves of the lower extremities are more frequent and more severe than those of the upper extremities. The posterior tibial nerve is most usually affected by leprosy, followed by the ulnar, median, lateral popliteal, and facial nerves, which causes numbness at the bottom of the foot. The major auricular and radial nerves are two additional nerves impacted by leprosy. Disabilities and deformities are caused by the disease's impact on the nerves.[1] Mononeuropathy multiplex is the most typical clinical form of nerve injury. During disease progression, the combined injury and regenerative process can develop into a pattern of nerve involvement resembling polyneuropathy (PNP), and is known as "mosaic polyneuropathy". The superficial sural and radial nerves are the nerves that are most frequently impacted, according to recent studies. However, involvement of this nerve frequently does not result in a clinical symptom, and leprosy patients are not regularly checked for its function. Nerve damage becomes far more severe when sensory loss causes unconscious stress. It's crucial to identify nerve involvement in leprosy cases as soon as possible.[2]

World Health Organization (WHO) has divided the degree of disability in patients with leprosy into 3, namely: grade 0 - there is no disability, grade 1 - lack of sensation in the feet or hands, grade 2 - defects that can be seen immediately such as ulcers on the feet and hands, muscle paralysis (foot drop and claw hand) or partial reabsorption of the fingers, as well as blindness. Since practically all leprosy patients encounter limits in their abilities to participate in society and the workplace owing to rejection and negative stigma, visible physical disability (grade 2 disability) is a significant issue for sufferers.[20] Silent neuritis is a clinical term for neuropathy accompanied by motor and/or sensory nervous system damage but without complaints of pain, numbness, or thickening of the nerves and no obvious signs of reaction. Silent neuritis is difficult for patients to detect, so that periodic examination of nerve function both during and after MDT treatment is important to do.[1] Richardus *et al.* in Bangladesh

found that 86% of leprosy patients had grade 2 disability due to silent neuritis without skin lesions or pain.[21] Most of participants in this study who were leprosy neuropathy patients did not have a grade 2 leprosy disability according to WHO (90.5%). This shows that there is a chance that if the neuropathic condition in leprosy can be treated quickly, then level 2 disability can be avoided.

Conclusion

In this research, the predominance of sociodemographic characteristics were found in the age range 18-35 years (57.1%), male (85.7%), secondary education level (57.1%), and work as employee (33,3%). The majority of the research subjects were MB type leprosy (100%), were experiencing leprosy reactions (42.9%), had RFT (47.6%), leprosy duration >12 months (57.1), had experienced symptoms of neuropathy (95.2%), duration of neuropathy symptoms ≤1 year (52.4%), location of neuropathy in the lower bilateral extremities (52.4%), and did not have a grade 2 leprosy disability (90.5%).

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