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Characteristics of neuropathic pain in Indonesia: A hospital based national clinical survey

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Abstract

We conducted a hospital based study to collect data on the clinical characteristics of neuropathic pain (NP) patients in neurology outpatients in 13 big cities in Indonesia. We aimed to identify the clinical characteristics of NP among patients with the symptoms of pain. A simple questionnaire was conducted to explore the clinical symptoms and signs. Participants who reported of NP symptom was 1,779 (21.8%) among 8,160 patients. The higher prevalence of NP was reported in 41-60 years old (n= 1,030; 57.9%). It was more prevalent in male (n=1,104; 62.1%). The group of patients with low educational level has higher prevalence of pain with NP (n=1,177; 66.1%). There are five main clinical symptoms of NP patients, pinprick sensation (n=589; 33.1%), electric shock like sensation (n=542, 30.5%), burning (n=407, 22.9%), paresthesia (n=401; 22.5%) and hyperalgesia (n=351, 19.7%). In this study, NP was mostly associated with low back pain (n=509, 28,6%), carpal tunnel syndrome (n=343; 19.3%), frozen shoulder syndrome (n=191, 10.7%), diabetic neuropathy (n=170, 9.6%) and brachialgia (n=108, 6.1%). The most frequent modality to treat NP symptoms were adjuvant analgesics, antidepressants or anticonvulsants (n=1,199; 67.4%), non-steroidal anti-inflammatory drugs (n=1,177, 66.2%), non-opioids analgesics (n=606; 34.1%), non-pharmacological treatment (n=366; 20.6%) and opioid treatments (n=100, 5.6%).

INTRODUCTION

Indonesia is a big country with total population of 252,124,458 in 2014. Ratio of primary health clinic is 1.08 per 30,000 populations. Total number of hospital is 2,408 and ratio of beds was 1.07 per 1,000 populations. Total general practitioner was 40,787 and total specialist was 46,994. The health facility is not equally distributed. A new health system was implemented in Indonesia since 2013 termed *Jaminan Kesehatan Nasional* (National Health Insurance). In December 2014 total 53% populations were covered by the National Health Insurance, 1,613 (67%) hospitals were connected with the National Health Insurance. The referral health system is implemented in National Health System. Chronic Pain is the most common reason for visiting the outpatient clinic (number one of 10 common diseases) and pain is a common symptom that was referred to neurologist.[1]

Neuropathic pain (NP) is a common symptom in neurology clinics. It can have a significant impact on a person's quality of life because of its chronicity and difficulty to treat. NP develops as a result of damage to, or dysfunction of the system that normally signals pain. It may arise from disorders that affect the peripheral and or central nervous systems. NP is very challenging to manage because of the heterogeneity of its etiologies, symptoms and underlying mechanisms.[2] Major causes of NP include: diabetes, carpal tunnel syndrome, spinal cord injury, stroke, multiple sclerosis, cancer, and HIV infection, as well as common conditions, such as lumbar or cervical radiculopathies, and traumatic or postsurgical nerve injuries.

Typical descriptions of the pain include terms such as shooting, stabbing, electric shock like sensation, burning, tingling, tight, numb,

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prickling, itchy and a sensation of pins and needles. People may also describe symptoms of allodynia (pain caused by a stimulus that normally does not provoke pain) and hyperalgesia (an increased response to a stimulus that is normally painful).[3]

NP is often difficult to treat, because it is resistant to many medications and/or because of the adverse effects associated with effective medications. Many people require treatment with more than one drug, but the correct choice of drugs, and the optimal sequence for their use, has been unclear. Clinicians may be guided by a number of published guidelines and algorithms for the management of NP, but these are not consistent regarding the choice of drug treatment. Some study showed the nonspecificities of NP pathophysiological mechanisms and its diagnostic underestimation, particularly in patients having no definite neurological condition.[4]

There have been considerable advances in the understanding of NP syndromes but there is still a lack of general epidemiological information. The exact prevalence of NP is not known.[5] The large range of etiologies indicates that the prevalence of NP may be high in neurology clinics but the characteristics is still unclear. A review of the epidemiology of chronic pain found that there is still no accurate estimate available for the population prevalence of NP [6] Two population-based studies from Europe reported the prevalence of pain of predominantly neuropathic origin[7] or pain with neuropathic characteristics[8] to be 8% and 7%, respectively. A German study reported that 37% of patients with prolonged low back pain had predominantly neuropathic pain.[9]

One major reason for the absence of hospital-based epidemiologic data on NP was the lack of physician's awareness, or simple clinical instrument that can identify the characteristics of NP. The aim of this study was to identify the most frequent clinical characteristic of NP among neurology outpatients who come with the symptoms of pain.

METHODS

A simple questionnaire was conducted to explore the clinical symptoms and signs. It is based on validated questionnaires including *Douleur Neuropathique en 4* Questions (DN4)[10], Leeds Assessment of Neuropathic Symptoms and Signs score (S-LANSS)[11] and any other clinical manifestations. Multicenter Hospital-based survey was carried out from July to December 2012 in 13 hospitals in Indonesia. This study has been approved by Ethic Committee, Sanglah Hospital Denpasar Bali. This survey was conducted by neurologists who provide out-patients and in-patients consultations in pain management.

This is a 6 months prospective study of the prevalence of NP and the clinical characteristics. All pain patients who came to neurology clinics in the first time were enrolled as subjects in this study. The recruited individuals were then subjected to face-to-face interviews. A simple questionnaire was used as a guidance to find clinical characteristics of patients. Detailed information from patients with NP was collected. Diagnosis of NP was based on physicians` clinical judgments. Data collected include the patients` demographic profiles, history of diseases, pain diagnosis and severity of pain (visual analogue scale) and treatment modality. Data was analyzed descriptively.

RESULTS

From 1 July 2012 until 31 December 2012, 8,160 subjects who reported of pain were enrolled in this study. Demographic data and characteristics of NP were shown in Table 1. Of these 8,160 patients, 1,779 patients (21.8%) had at least one symptom of neuropathic pain, while the other 6,381 patients (78.2%) had symptoms of non neuropathic pain (Table 1). Prevalence of neuropathic pain was higher in male than in female (62.1% vs 37.9%).

A total of 81% (1,441) subjects were Javanese and Balinese and 338 (19%) were the other ethnic groups. Forty to sixty year old patients were the most frequent age group in this study (57.9%), followed by less than 40 year old (24.85%) and more than 60 year old (17.26%). The subjects with neuropathic pain in this study were predominantly male, middle aged and having low back pain. Two thirds (i.e. 66%) of the subjects have low educational level (less than 6 year), and only 11% of the subjects have high educational level (more than 12 years). Low income people are majority in this study (70%).

Low back pain (n=509; 28.6%), was the most common concomitant condition with neuropathic pain, followed by carpal tunnel syndrome/CTS (n=191; 10.7%), frozen shoulder (n=191; 10.7%), diabetic neuropathy (n=170; 9.6%) and brachialgia (n=108; 6,1%).

About three-quarters (73.4%) of respondents reported severe pain intensity (visual analogue scale/VAS score ≥7), 32.3 % reported moderate

TABLE 1: Demographic data and characteristics of neuropathic pain of the study subjects

Variable	Number of patients (8,160)	Percent
Types of pain		
- Neuropathic	1,779	21.8
- Non neuropathic	6,381	78.2
Gender		
- Male	1,104	62.1
- Female	675	37.9
Age		
- < 40 years	442	24.8
- 40-60 years	1,030	57.9
- > 60 years	307	17.3
Educational level		
- Low	1,177	66
- Middle	409	23
- High	196	11
Sosioeconomic level		
- Low income	1,288	70
- Middle-high Income	541	30

pain intensity (VAS 4–6) and 1.1% reported mild pain (VAS < 4).

The five most dominant clinical symptoms among neuropathic patients were pinprick sensation (n=589; 33.1%), electric shock like sensation (n=542; 30.5%), burning sensation (n=407; 22.9%), paresthesia (n=401; 22.5%) and hyperalgesia (n=351; 19.7%). The clinical manifestations are shown in Table 2.

The common therapy of neuropathic pain in this study was pharmacological treatments. The most frequent modality to treat neuropathic symptoms was adjuvant analgesics, antidepressants or anticonvulsants (n=1,199; 67.4%), non-steroidal anti-inflammatory drugs (NSAIDs, n=1,177; 66.2%), non-opioid analgesics (n=606; 34.1%), non-pharmacological treatments (n=366; 20.6%) and opioid treatments (n=100, 5.6%). Only 22.6 % of patients were referred to physiotherapists. The types of medications commonly prescribed by pain specialists for NP relief are shown in Table 3.

DISCUSSION

This survey is a first national hospital based study of NP in Indonesia. The strength of this study was the large size of the sample from hospitals widely

Table 2: Clinical manifestations of study subjects with neuropathic pain

Symptoms	No. of patients (n = 1779)	Percent
Pinprick sensation	589	33.1
Electric shock like sensation	542	30.5
Burning sensation	407	22.9
Paresthesia	401	22.5
Hyperalgesia	351	19.7
Lancinating	126	7.0
Hypoesthesia	89	5.0
Cold	60	3.0
Allodynia	52	2.9
Causalgia	34	1.9
Dysesthesia	7	0.4

Table 3: Treatment modality of the patients with neuropathic pain

Modality	Number of treatments (n=1779)	Percent
Analgesics adjuvants	1,199	67.4
NSAIDs	1,177	66.2
Analgesics non-opioid	606	34.1
Non-pharmacological treatments	366	20.6
Opioid treatments	100	5.6

NSAIDs, non-steroidal anti-inflammatory drugs

distributed in Indonesia. Demographic data and characteristics of NP of this study were shown in Table 1. Total subjects who reported pain were 8,160. Of these patients, 1,779 patients (21.8 %) had at least one symptom of NP, while the other 6,381 patients (78.2%) had symptoms of non NP (Table 1). Some studies reported a relatively large range of prevalence rates of chronic NP (i.e. 7-50%).[8] Our result was lower than in the Siriraj Hospital Thailand, that showed 37.8% of patients came to the pain clinics were diagnosed as having NP. It maybe caused by referral bias (pain clinic in Siriraj Hospital and neurology clinic in this study). Another possible reason is Siriraj pain clinic tends to have chronic and severe pain cases, especially terminal cancer cases, which has been shown to have higher prevalence of neuropathic pain.[8,9]

Prevalence of NP was higher in male than in female (62.1% vs. 37.9%). This data was different from the other population based study that found higher prevalence of NP in female.[13] The high proportion of male patients is probably correlated with the most common cause of NP in this study of low back pain. Risk of low back pain is higher in men than women. The most common cause of low back pain is non specific/mechanical, most commonly found in men. Also, male patients in productive age tend to seek medication for financial reason, which could possibly cause higher prevalence of male patients in our study.

Forty to sixty year old patients are the most frequent in this study (57.9%), followed by less than 40 year old (24.85%) and more than 60 year old (17.26%). This pattern is different with the other study that showed significant increase of NP with age.[12] Subjects with NP in this study were predominantly male, middle aged and having low back pain.

Two thirds (i.e. 66%) of the subjects have low educational level (less than 6 year), and only 11% of the subjects have high educational level (more than 12 years). Low income people are majority in this study (70%). Low income is defined as income less or equal to regional minimum wage. Middle high income is defined as income more than regional minimum wage. This study is similar with the other study that also found that educational level and socioeconomic status were also important risk factors. Patients at the lower socioeconomic and educational level were associated with more chronic pain.[13] Low income level can correlate with the risk of some diseases like back pain, carpal tunnel syndrome (CTS), frozen shoulder, and brachialgia.

NP is a heterogeneous group of conditions that differs not only in etiology but also in location. We found that low back pain (n=509; 28.6%), was the most common concomitant condition with NP, followed by CTS (n=191; 10.7%), frozen shoulder (n=191; 10.7%), diabetic neuropathy (n=170; 9.6%) and brachialgia (n=108; 6.1%). Entrapment neuropathy or nerve compression was dominant in this study. Most other studies found that the anatomical sites of lesion causing NP was multiple and those most commonly affected were the distal extremities. They also reported that diabetes, immune deficiencies, malignant diseases, spine and ischemic disorders might all give rise to NP.[14] In this study, the most frequent combinations in participants with neuropathic characteristics were pain in the lower limbs and the back (low back pain) or in the upper limbs and the neck (CTS, frozen shoulder, brachialgia).

These specific distributions might indicate that the neuropathic characteristics in this study corresponded primarily to lumbar or cervical radiculopathies and maybe related to occupation. This result is consistent with the data showing that chronic back and neck pain was highly prevalent in the general population.[9] The prevalence of NP among adult with chronic low-back pain in the Arabian Gulf region from the outpatients assessed using the LANSS was 55%.[14]

Proportion of patients who suffered from severe pain is common in this study (73.4%).

About three-quarters (i.e. 73.4 %) of respondents reported severe pain intensity (visual analogue scale/VAS score ≥7), 32.3 % reported moderate pain intensity (VAS 4–6) and 1.1% reported mild pain (VAS < 4). In the other population study, the prevalence of moderate to severe pain was 19.9% for chronic pain.[8] These data indicate that most patients who sought treatment in our clinics have moderate to severe pain. It is possible that those with less pain self-medicate, or sought treatment elsewhere.

The five most dominant clinical symptoms among neuropathic patients were pinprick sensation (n=589; 33.1%), electric shock like sensation (n=542; 30.5%), burning sensation (n=407; 22.9%), paresthesia (n=401; 22.5%) and hyperalgesia (n=351; 19.7%). The results of the study conducted by Boureau *et al*.[15] provided evidence that six terms were significantly more frequently chosen by patients with NP. These six terms were electric shock, burning, cold, pricking, tingling and itching. The six most dominant clinical symptoms among neuropathic patient in this study were pinprick sensation, electric shock like sensation, burning sensation, paresthesia, hyperalgesia, and lancinating pain. These characteristics provide important support for clinical observations that these pain descriptions are particularly valuable in identifying patients with NP.[15]

There is possibility to screen the different symptoms of NP according to these clinical symptoms. The result showed that by using the specific pain descriptors such as pinprick, electric-shock like, burning, paresthesia, hyperalgesia and lancinating pain, the questionnaire could diagnose patients with NP. However, a study by Rasmussen *et al*. reported that the use of pain descriptors could not distinguish between the three clinical categories: "definite neuropathic pain", "possible neuropathic pain" and "unlikely neuropathic pain".[15]

In general practice, pharmacotherapy remains the mainstay of neuropathic management. The most frequent modality to treat neuropathic symptoms in this study was adjuvant analgesics, antidepressants or anticonvulsants (67.4%), NSAIDs (66.2%), non-opioid analgesics (34.1%), non-pharmacological treatments (n=366; 20.6%) and opioid treatments (n=100, 5,6%). Medical therapies for NP tend to involve drugs whose primary indication is not analgesia, such as anticonvulsants and antidepressants. The available evidence for the efficacy of these drugs has been repeatedly reviewed. The high usage of antidepressants and anticonvulsants not only reflects the nature of NP, for which these groups of medications are more effective, but also the complexity of chronic pain management where a combination therapy may be necessary to provide adequate pain relief.[15]

The strength of this study is that it utilized questionnaire adapted from validated instrument like DN4 questionnaire and LANSS. This instrument has been formally validated in the clinical setting to identify neuropathic pain characteristics. The volume of data was also large enough to reflect the profiles of NP patients.

In conclusion, this large national hospital based study indicates that a significant proportion of patient reported NP were male, middle aged and having low education level. Pinprick and electric shock like sensation were the most common symptoms in neuropathic patient. Physicians should aware of low back pain and carpal tunnel syndrome as causes of neuropathic symptoms. The most frequent modality treatment in neuropathic symptoms is adjuvant analgesics and NSAIDs.

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