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PAIN DETECT AS A TOOL FOR THE SCREENING OF NEUROPATHIC PAIN IN PATIENTS WITH DIABETES MELLITUS

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ABSTRACT

Background: Diabetic neuropathy (DN) is a prevalent long-term complication of diabetes mellitus (DM), affecting more than 50% of patients. In addition, several studies also showed that distal symmetric polyneuropathy (DSPN) accounts for 75% of all DN cases. To facilitate the treatment of DN, painDETECT questionnaire, a self-reported tool with 85% sensitivity and 80% specificity, has been recommended for detecting neuropathic component in pain.
Objective: This study aimed to promptly diagnose DN using painDETECT questionnaire in DM patients.
Methods: The study procedures were carried out using a descriptive, cross-sectional design with 67 DM patients from Cibabat Regional Hospital Department of Internal Medicine outpatient clinic through consecutive sampling in October–November 2022. Primary data were obtained using the adapted and validated Indonesian painDETECT questionnaire.
Results: Among the 67 patients, 32.9% experienced neuropathic pain with a score of 19–38, indicating the involvement of >90% of neuropathic pain components. Sensory deficits, such as numbness, burning sensation, pins-and-needles, and allodynia, were observed in 86.3%, 90.1%, and 72.7% of patients with neuropathic pain, respectively. In addition, a total of 59.7% of participants (n=40) reported the presence of mild pain (NRS 3).
Conclusion: Based on the results, the majority of patients had complaints of neuropathic or mild pain (40 subjects; 59.7%). Among the 22 patients experiencing neuropathic pain, 54.5% reported mild intensity.

Keywords: diabetes mellitus, diabetic neuropathy, polyneuropathy

Introduction

Diabetes Mellitus (DM) is a metabolic disease characterized by hyperglycemia due to disorders in insulin secretion, insulin function, or both.[1] According to a 2021 survey by the International Diabetes Federation (IDF), Indonesia has the fifth-highest number of adults with DM, totaling approximately 19.5 million patients. Projections also suggest that this figure can increase to 28.6 million patients by 2045.[2] In addition, Indonesia currently ranks as the country with the third-highest number of undiagnosed adult DM. This indicates that tens of millions of undocumented patients are not included in the published statistics.[2] Several studies have shown the complications of type 2 DM can be divided into 2 categories, namely vascular and nonvascular.[1,3]

Vascular complications are further subdivided into microvascular, consisting of retinopathy, neuropathy, and nephropathy, as well as macrovascular, comprising coronary artery disease, peripheral artery disease, and cerebrovascular disease.[1,3] Meanwhile, nonvascular complications have been reported to comprise infections, skin changes, and hearing loss.[3] In line with previous reports, diabetic neuropathy (DN) is one of

the long-term complications of DM with more than 50% of DM experiencing the condition. The Special Interest Group on Neuropathic Pain (NeuPSIG) of the International Association for the Study on Pain (IASP) defined neuropathic pain as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system", including both the central and peripheral system. This condition has the potential to lower patients' quality of life and typically requires long-term therapy, thereby differing from non-neuropathic pain.[4-7] In addition, distal symmetric polyneuropathy (DSPN) constitutes 75% of all DN. IASP defines DSPN as pain arising as a direct consequence from disorders in the tissue of the peripheral somatosensory system in DM patients, predominantly affecting the legs and feet.[8] The diagnosis in clinical setting often depends on patients' description of pain.

Classic symptoms of painful DN include distal symmetrical pain, often worsening at night and described as shooting, stabbing, electric shock-like, and burning. Clinical examination usually reveals hyperalgesia and allodynia, along with persistent numbness, pins-and-needles sensation, and disabling shooting pain. This condition often indicates distal symmetric sensorimotor neuropathy, characterized by the involvement of small and large nerve fibers (mixed sensorimotor). Initially, the most distal parts of the extremities are affected, causing characteristic "glove and stocking" loss of sensation. Previous studies also reported the presence of abnormalities in sensation of light touch, sensitivity to pressure and vibration, as well as joint proprioception, and reduction or absence of ankle reflex. The symptoms are known to appear at night and affect patients' quality of life in multiple aspects, including mobility, work, sleep, mood, self-regard, recreation, and social activities.[9]

As diabetic neuropathy advances, patients face higher financial burdens and healthcare professionals encounter significant challenges. This underscores the urgent need for accurate, rapid, and cost-effective detection, especially in resource-limited healthcare settings where timely diagnosis is crucial for successful treatment. One potential screening tool for detecting neuropathic pain component is painDETECT questionnaire. The questionnaire was initially developed for use in cases of low back pain, but has shown promise in broader applications and has been translated into Indonesian. Studies exploring the diagnostic potential of self-reported painDETECT scores have reported a sensitivity of 85% and a specificity of 80%. Therefore, this study aims to the detection of neuropathic pain among patients with DM polyneuropathy using painDETECT questionnaire at Cibabat Regional Hospital in Cimahi, Indonesia.

Methods

This descriptive study was carried out using a cross-sectional design, comprising a total of 67 patients with DM at Cibabat Regional Hospital Department of Internal Medicine outpatient clinic. In addition, participants were selected using consecutive sampling from October to November 2022. Primary data were collected through responses on the adapted and validated Indonesian painDETECT, while secondary data were extracted from medical records. The inclusion criteria comprised patients with DM visiting Cibabat Regional Hospital Department of Internal Medicine outpatient clinic, who willingly agreed to participate. Meanwhile, the exclusion criteria included individuals with mental disorders, communication difficulties, dementia, pregnancy, and those who declined participation. Sample characteristics, including age, sex, and duration of DM, were then examined.

The painDETECT questionnaire comprised a series of questions that determined the variety of pain patients could feel. This included location, fluctuation, characteristics, and the different types of pain. painDETECT questionnaires offered a series of levels that were added up into a scoring system. The score was then categorized as nociceptive pain (score 0-12), unclear pain (13-18), or neuropathic pain (19-38). Nociceptive pain was with minimal neuropathic pain, while pain that was unclear was considered ambiguous with neuropathic components. Neuropathic pain showed that this pain most likely comprised neuropathic components. The data obtained were analyzed using SPSS version 25. Ethical clearance for this study was granted by Cibabat Cimahi Regional Hospital Ethics Committee (No. 070/20/Ethical Clearance/RSUDCibabat/XI/2022).

Results

This section provides a comprehensive overview of the mean age characteristics of the participants enrolled in this study. It includes detailed demographic information, such as the distribution of age across different groups of participants, potentially stratified by factors like gender, comorbidities, or other relevant variables. Additionally, it explores any notable trends or variations in age distribution between participants with and without neuropathic pain, offering valuable insights into how age may influence pain perception, progression, and management. These findings contribute to understanding the role of age in the context of neuropathic pain among individuals with DM polyneuropathy (Table 1).

Table 1. Subject characteristics

Variable	n = 67
Age (year)	
30–45	4 (6%)
46–60	30 (44.8%)
>60	33 (49.2%)
Sex	
Male	26 (38.9%)
Female	41 (61.2%)
Duration of DM	
<5 years	32 (48%)
>5 years	35 (52.2%)
Neuropathic pain	22 (32.9%)
Non-neuropathic pain	45 (67.2%)
Medications	
Oral hypoglycemic agents	24 (35.8%)
Insulin	43 (64.2%)

Table 2. Mean painDETECT scores of the subjects

Variable	n = 67
Score	
0–12 (nociceptive)	18 (26.8%)
13–18 (unclear)	27 (40.2%)
19–38 (neuropathic)	22 (32.8%)

The mean painDETECT scores obtained from the participants, offering a quantitative measure of neuropathic pain symptoms. This table likely provided a breakdown of the painDETECT scores across different subgroups or categories within the study population, shedding light on the prevalence and severity of neuropathic pain experienced by the participants (Table 2).

Table 3. Pain Characteristics of the Subject

Variable	Nociceptive Pain	Unclear	Neuropathic Pain	P Value
Age				0.989*
- 30-45	1 (35.0)	2 (50.0)	1 (25.0)	
- 40-60	7 (25.0)	11 (39.3)	10 (35.7)	
- >60	9 (28.1)	12 (37.5)	11 (34.4)	
Sex				0.176*
- Men	6 (23.1)	8 (30.8)	12 (46.2)	
- Women	12 (29.3)	19 (46.3)	10 (24.4)	
Duration of DM				0.139*
- <5 years	11 (34.4)	9 (28.1)	12 (37.5)	
- >5 years	20 (18)	18 (51.4)	10 (28.6)	
Pain Intensity				0.000*
- Mild (n(%))	18 (43.9)	22 (53,7)	1(2.4)	
- Moderate (n(%))	0 (0.0)	5 (23.8)	16 (76.2)	
- Severe (n(%))	0 (0.0)	0 (0.0)	5 (100.0)	
Sensation of Radiating Pain				0.000*
- Yes	0 (0.0)	0 (0.0)	17 (100.0)	
- No	18 (36.0)	27 (54.0)	5 (10.0)	
Pain Pattern				0.000*
- Persistent pain with slight fluctuations	6 (100.0)	0 (0.0)	0 (0.0)	
- Persistent pain with pain attacks	10 (100.0)	0 (0.0)	0 (0.0)	
- Pain attack without pain in between	1 (6.7)	14 (93.3)	0 (0.0)	
- Pain attacks with pain in between	1 (2.8)	13 (36.1)	22 (61.1)	
Burning Sensation[a]	0 (0-1)	0 (2-4)	1 (3-5)	0.000*
Pins and Needlesa[a]	0 (1-3)	1 (3-5)	1 (3-5)	0.000*
Allodynia[a]	0 (0-0)	1 (2-5)	1 (3-5)	0.000*
Electrical Shock-like Pain[a]	0 (0-1)	1 (0-5)	0 (3-5)	0.000*
Sensitive to Temperature[a]	0 (0-0)	0 (0-2)	2 (0-4)	0.000*
Changes[a]				
Numbness[a]	0 (0-0)	3 (0-4)	0 (3-5)	
Tenderness[a]	0 (0-1)	0 (0-1)	0 (0-1)	

*uji Chi-square, ** Kruskall-Wallis
[a](median (minimum-maximum))

There were no significant differences regarding nociceptive pain and neuropathic pain with variables of age, sex, and the duration of DM (p-value> 0.05). However, the pain intensity, sensation of radiating pain, and pain patterns were statistically significant (Table 3).

Discussion

This was the first study to use painDETECT as a screening tool for neuropathic pain in DM patients. Sofyan et al. previously used painDETECT questionnaire to screen for neuropathic pain in 57 patients with cancer pain at Cipto Mangunkusumo National General Hospital and neurology outpatient of Dharmais Hospital. The results showed that the proportion of neuropathic pain in patients with cancer pain was 31.6%, all of which were patients with metastasis. In patients with neuropathic pain, the pain was felt as severe and radiating. All patients had sensory defects of numbness and 83.3% experienced burning, pins, and needles in the cancer sites.[15] A study conducted at the Internal Polyclinic of Cibabat Hospital showed that 32.9% of patients had neuropathic pain, where 54.5% experienced pain with mild intensity. Patients with neuropathic pain experienced sensory deficits of numbness and burning (86.3%), tingling sensation (90.1%), and allodynia (72.7%). The Indonesian painDETECT had been proven to be valid in line with ISPOR transcultural adaptation guidelines. This was supported by the retest test, which caused painDETECT questionnaire to have good feasibility in screening for neuropathic component.[11] Statistical analysis conducted in the Internal Medicine outpatient of Cibabat Regional Hospital showed that a majority of patients had mild pain (NRS 3). Wahyuni et al. (2021) also reported that a majority of participants (61.6%) experienced mild neuropathy. In this study, the majority of participants were female (61.2%). Franconi et al. in 2012 theorized that the difference in estrogen caused females to be at a higher risk of peripheral neuropathy.[16] The results revealed that there was no difference in the incidence of neuropathy between patients with DM duration of >5 years or <5 years. This could be due to most patients having already experienced symptoms of neuropathy during the first diagnosis.

Rahmawati et al. in 2018 stated that there was no correlation between the duration of DM and the incidence of peripheral neuropathy. The duration of DM and HbA1c concentration were the main predictors of DN. These 2 predictors were generally associated with other metabolic factors, specifically type 2 DM, such as insulin resistance and hypertension. In population-based studies from multiple countries, including the United States, Denmark, China, and the Netherlands, obesity occurred frequently in patients with neuropathy.[17] The majority of patients with neuropathic pain were affected at both distal extremities. This condition was typically distal symmetrical sensorimotor neuropathy. Other clinical characteristics were due to the involvement of small and large nerve fibers (mixed sensorimotor). Initially, the distalmost parts of the extremities were affected, causing glove and stocking sensory loss, which showed the involvement of the longest nerve fibers. Early symptoms presented nocturnally and affected patients' quality of life overall, including mobility, work, sleep, mood, self-regard, recreation, and social activity.[18]

Patients with neuropathic pain were managed by a multidisciplinary team. First-line treatment of pain, including chronic pain, was often pharmacotherapy. However, neuropathic pain differed from musculoskeletal pain, and analgesics commonly used, such as opioids were not suitable or as effective in managing chronic neuropathic pain, including DN. Approved and used pharmacological agents to treat DN were mostly not traditional analgesics or opioids consumed "as needed" but were instead agents, such as anticonvulstans and antidepressants, which must be routinely consumed for a certain amount of time to achieve maximal effect. Physicians also had to consider specific patient factors, such as age, quality of life goals, functional status, and comorbidities when determining the appropriate management.[19] Duloxetine and pregabalin were the only drugs to gain approval from the Food and Drug Administration to treat DM polyneuropathic pain.[20] In the United Kingdom, the National Institute for Health and Care Excellence recommended amitriptyline, duloxetine, pregabalin, and gabapentin as first-line treatments for neuropathic pain.[21] Investigating neuropathic pain in diabetes using other methods is encouraged, given the painDETECT's sensitivity and specificity of 85% and 80%, respectively. This study may serve as a reference for future reports on neuropathic pain in diabetes.[21]

The limitations of this study were related to unique use of the painDETECT questionnaire as a screening tool for neuropathic pain in DM patients. While the Indonesian painDETECT was valid according to ISPOR transcultural adaptation guidelines, the study was conducted in a specific outpatient setting at Cibabat Regional Hospital, limiting results to broader populations or different healthcare settings. Additionally, the study focused on DM patients from a single region, and factors such as age, gender, and diabetes duration could vary across populations. The absence of a comparison with alternative neuropathic pain methods was another limitation. The management approach, involving a multidisciplinary team and specific pharmacological agents, may not be universally applicable due to regional differences in healthcare practices and drug approvals. Caution is needed when extrapolating these results, and further studies with varied methodologies are recommended to better understand neuropathic pain in DM populations.

Conclusion

In conclusion, the application of painDETECT questionnaire could represent an important step forward in the assessment and understanding of neuropathic pain in DM patients. By identifying a significant proportion of DM patients experiencing neuropathic pain, early detection and intervention was essential in managing the condition. Several limitations must also be acknowledged, such as the study's reliance on a specific outpatient setting and the absence of comparisons with alternative assessment methods. In addition, the focus on a single region and the specific management approach could limit generalizability to broader populations and healthcare contexts. Despite the limitations, this study provided valuable insights and served as a foundation for further reports aimed at improving the management of neuropathic pain in DM populations.

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