BMJ Open Prevalence, discomfort and self-relief behaviours of painful diabetic neuropathy in Taiwan: a cross-sectional study

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ABSTRACT
Objectives: To explore the prevalence, discomfort, and self-relief behaviours of painful diabetic neuropathy (PDN) among rural community residents with type 2 diabetes.

Design: A community-based, cross-sectional study.

Setting: This study was part of a longitudinal cohort study of a nurse-led health promotion programme for preventing foot ulceration in Chiayi County, Taiwan.

Participants: Six hundred and twenty-eight community adults with type 2 diabetes participated in this study.

Outcome measures: Parameters assessed included peripheral neuropathy, peripheral vasculopathy, glycaemic control and metabolic biomarkers. Statistical analyses included descriptive statistics and a multivariate logistic regression model.

Results: About 30.6% of participants (192/628) had PDN. Factors associated with PDN included an abnormal ankle brachial index (ABI; OR=3.4; 95% CI 1.9 to 6.2; p<0.001), Michigan neuropathy screening index (OR=1.69; 95% CI 1.0 to 2.6; p=0.021), triglyceride level (OR=1.61; 95% CI 1.0 to 2.4; p=0.036) and being female (OR=1.68; 95% CI 1.1 to 2.4; p=0.022). PDN was characterised by uncomfortable feelings of prickling, stinging or burning pain and inexplicable dullness around the base or dorsal areas of the feet, but received little attention or treatment from primary healthcare providers.

Conclusions: A high prevalence of PDN was found in rural community residents with type 2 diabetes and the healthcare workers provided little attention to, or treatment of, discomfort. It is important to identify high-risk groups with PDN early in order to prevent foot ulceration and reduce the incidence of amputation of the extremities. It is also urgent to develop appropriate treatment and self-relief behaviours to halt or reverse the progression of PDN for this population living in rural areas.

INTRODUCTION
The World Health Organization reported that 347 million people worldwide had diabetes in 2008,1 and it was postulated that this would increase by 50% in Asia, the Middle East and Africa by 2030.2 In Taiwan, type 2 diabetes is the fourth leading cause of death with a standardised mortality rate of 26.9/105, which is higher than Korea (21.8/105), the USA (14/105), Singapore (13.4/105), the UK (5.0/105) and Japan (4/105).3 Researchers have indicated that diabetic peripheral neuropathy (DPN) is a common complication of diabetes and represents a major health problem, including diabetic foot ulceration.1,5 Painful diabetic neuropathy (PDN) is one of several clinical syndromes in patients with DPN and presents a major challenge for optimal management.6 Some studies have described the symptoms of PDN as a superficial burning pain around the feet and lower extremities and a serious disruption of social functioning and mood. Unlike physiologic pain, neuropathic pain is not self-limiting and not easily...
treated. However, little is known about the prevalence, patient discomfort and factors associated with PDN in Taiwan, which, in the rural areas, is known to have a high prevalence of type 2 diabetes and foot ulceration.

DPN affects approximately 30–50% of patients with diabetes. It is estimated that 40–60% of patients with DPN develop PDN in their lower limbs. Similar to other conditions of neuropathic pain, PDN seems to progress and is often under-reported and difficult to diagnose and treat. The net result can be intolerable pain, substantial morbidity and erosion of the quality of life of patients with PDN. It is also important to consider how these patients adapt to, or self-relieve, their painful conditions because some of their behaviours might be associated with, or contribute to, the risk of secondary complications, such as diabetic foot ulcerations, which are a major cause of lower extremity amputations.

Researchers have indicated that PDN primarily involves symmetrical, length-dependent, sensorimotor polyneuropathy attributable to metabolic and microvascular alterations, affects small and/or large sensory fibres and progresses gradually from the distal limbs. Although the efficacy of pharmacological (eg, tricyclic antidepressants, selective serotonin reuptake inhibitors, anticonvulsants and antioxidants such as d-lipoic acid) and non-pharmacological (eg, spinal cord stimulation modalities) treatments for PDN appear to be promising, its management still poses a unique challenge owing to the variability in symptoms and responses to treatments. Therefore, identification of modifiable factors of PDN is necessary for the development of early and effective prevention to halt or reverse its progression. In addition, while numerous risk factors for DPN have been identified (ie, hyperglycaemia and cardiovascular and metabolic factors), the associated factors specific to PDN remain largely unexplored.

PDN might be a syndrome clinically distinct from DPN. Further investigations of the underlying mechanisms are necessary to determine whether the risk factors related to PDN are also associated with the onset and progression of PDN. Therefore, this study aimed to explore the prevalence, associated factors, discomfort and self-relief behaviours of PDN in Taiwanese rural residents with type 2 diabetes.

**Methods**

**Design, sample and setting**

This investigation formed part of a longitudinal cohort study of the effects of health promotion in preventing foot ulceration among rural community residents with type 2 diabetes. A community-based health screening survey was conducted between 2010 and 2015 using a cross-sectional descriptive design. The inclusion criteria were as follows: participants must (1) have been diagnosed with type 2 diabetes, reported discomfort, pain or numbness in the lower limbs and be identified by the research team; (2) have the ability to complete the questionnaires in Mandarin or a Taiwanese dialect by face to face interview and (3) agree to participate in the study and provide informed consent before participation. Exclusion criteria were (1) inability to complete the questionnaires and serious learning difficulties and (2) diagnosis of low back pain (eg, lumbar herniated intervertebral disc disease) and various other painful foot problems (eg, gout, osteoarthritis) or experiencing serious complications of diabetes (eg, foot ulceration and minor or major lower limb amputation).

We undertook a two-part approach to study the prevalence and discomfort of PDN. In part 1, the public health nurses in each of the 18 districts carried out a simple random sampling from their local diabetes registration files. According to the total annual quota for free check-ups by the Bureau of Health Promotion, each district was expected to select 40–50 samples for a total of 900 diabetic residents. For example, in the C district, 200 candidates in the diabetes registration file had a series number and so for this district four cases were selected. In part 2, the discomfort of patients with PDN was explored by a focus group discussion to which all participants were invited.

**Measurements**

1. **Peripheral neuropathy** was assessed with the reliable and valid Michigan neuropathy screening instrument (MNSI), consisting of five parameters: (a) appearance of the feet—inspection of the lower limbs for deformity; (b) foot ulceration; (c) semiquantitative assessment of vibration sensation on the dorsum of the big toe; (d) ankle reflexes and (e) touch-pressure sensation test. Each parameter was graded as 1, 0.5 or 0 with a total score ranging 0 from 10; a MNSI score >2.0 was defined as peripheral neuropathy. As an important indicator for the early detection of neuropathy, a semiquantitative assessment of vibration perception threshold was conducted with a 128 Hz turning fork on the dorsum of the big toe. A 5.07/10 g Semmes–Weinstein monofilament was applied perpendicularly to the test sites of the feet to assess touch-pressure sensation. The inter-rater agreement was 90% in this study.

2. **Peripheral vascular assessment** was measured using the ankle brachial index (ABI), which was calculated using ankle/arm pressure with the Cardio-Vision Model (MS-2000). ABI values ≥0.9 and <0.9 were classified as normal and peripheral vasculopathy, respectively.

3. **Glycaemic control and metabolic indicators** were measured using fasting blood glucose (FBG), glycohaemoglobin (HbA1C), triglyceride (TG) and total cholesterol (TC) levels, blood pressure and waist circumference (WC). The mean FBG, HbA1C, TC and TG values during 3 months were retrieved from the household computerised diabetes registries of each district. Blood pressure and WC were measured at the time of the study using standard procedures. WC (cm), a
4. Basic information and details of health-related behaviours were collected—namely, age, gender, education level, duration of diabetes, body height and weight, history of medication (ie, oral antidiabetes drugs and/or insulin) as prescribed by a physician and health habits (eg, smoking, exercise and wearing of adequate indoor/outdoor shoes). For smoking, participants were classified as ‘none or formerly’ if they had never smoked or had not smoked for 1 year or ‘current users’ if they were currently smoking. Participants who never or sometimes exercised were classified as ‘not often’ and those who usually exercised for a total of ≥30 min/day, three times a week, or 150 min/week were classified as ‘often’.3,5

5. PDN, discomfort and self-relief behaviours were evaluated using the following three structured and semistructured questions: (1) PDN was identified by the research team through a subjective question, “Do you have painful feeling on your feet?” and the answers were classified as “yes” or “no”. (2) “Please describe the feelings that you experienced in your leg(s): (a) How do you describe the most discomforting feeling in your leg(s)? (b) Where were the most uncomfortable areas? (c) When did you experience the most discomfort?” and (3) “Please describe how you dealt with or self-relieved the discomfort?”. Discomfort and self-relief behaviours were summarised as frequencies and percentages in all PDN participants.

Procedure and ethical considerations
Upon approval by institutional review boards, participants were recruited by their district public health nurses through regular home visits or by telephone. Participants were informed about the study and received an invitation letter with a brief explanation of the procedures and their opportunity to participate in the study. This study was conducted in collaboration with the Chiayi Bureau of Health Promotion. Potential participants were recruited through the invitation for free annual check-ups by the Department of Health Bureaus. Before the study, informed consent was obtained from each participant by the district public health nurse.

The research team included two physicians specialising in metabolic medicine and wound care, two graduate research assistants with registered nurse certification, 10 community volunteers and 18 public health nurses. To assure competency and reliability in delivering the research protocol, the primary investigator initiated three 6-hour training sessions, allowing all team members to familiarise themselves with the instruments, physiological measures and strategies for focus group interview before the start of the study. After the initial screening of PDN, all participants with evident symptoms or signs of the disease were invited to participate in part 2 of the study—the focus group interviews. All interviews were conducted by eight registered nurses certified as diabetic educators; each focus group discussion held at the local health centre included 6–8 participants and lasted for 30 to 45 min.

Statistical analysis
Data for demographics, physiological indicators and health-related behaviours were compared using a $\chi^2$ test (univariate analysis) between participants with and without PDN. To investigate factors associated with PDN, those variables significant in the univariate analysis ($p<0.05$) were incorporated into the multivariable logistic regression analysis with forward stepwise selection.31 No formal sample size determination and power analysis was carried out in this study because no previous studies had had an effect size calculation. Data analysis was performed using SPSS V.22 (IBM SPSS, Armonk, New York, USA: IBM Corp). All tests were two-sided and $p<0.05$ was considered to be statistically significant.

RESULTS
A total of 656 participants were initially enrolled during part 1 of the study; 28 of these left the research procedure owing to difficulty in maintaining contact, not undergoing the physiological measurements, or moving to another residence. Based on the criteria employed, 30.6% (192/628) participants had PDN and most were women (63%). The mean age of participants with PDN was 71 years and half of them had diabetes for >10 years (table 1). Approximately, 81.3% of participants completed elementary school. Participants in the PDN group reported less frequent and irregular exercise (53.6%) and abnormal values of MNSI scores (63%), systolic blood pressure (73%), central obesity (71%), HbA1C (63%) and FBG levels (61%).

According to the univariate analysis, participants with PDN were more likely to be women ($\chi^2=4.52; p=0.034$), have abnormal MNSI ($\chi^2=7.87; p=0.005$), ABI ($\chi^2=18.76; p<0.001$) and TG levels ($\chi^2=4.79; p=0.029$) and less likely to take part in exercise ($\chi^2=4.04; p<0.043$; table 1). After adjusting for potential confounders (including gender, age, education, smoking habits), the associated risk factors of PDN were abnormal ABI (OR=3.4; 95% CI 1.9 to 6.2; $p<0.001$), MNSI (OR=1.69; 95% CI 1.0 to 2.6; $p=0.021$), TG (OR=1.61; 95% CI 1.0 to 2.4; $p=0.036$) and being female OR=1.68; 95% CI 1.1 to 2.4; $p=0.022$), but not exercise behaviours (table 2).

During part 2 of the study, 192 participants with PDN were invited and all participated in the focus group interviews with agreement forms. A majority of participants used the following descriptions of PDN: “prickling and
stinging pain”, “dry and painful”, “burning pain”, “inexplicable dullness and excruciating pain” and “my legs do not belong to me” (table 3). Examples of participants’ responses included “Actually, I don’t know how to describe the uncomfortable and annoying feelings...it is just like a needle stinging or a knife stabbing your legs. The shooting pain is just below the legs”. The major discomfort areas perceived by the participants were “base and/or dorsum of the feet or toes” and the time of discomfort was reported to be “at night and during sleeping”, “anytime or all day long” and “during walking”.

The most frequently reported self-relief behaviours were “keep moving”, “don’t know what to do”, “trying domestic non-prescription products” and “seeking help”.

Table 1  Factors associated with painful diabetic neuropathy

| Variables                        | Painful diabetic neuropathy |       |       | χ²  | p Value |
|----------------------------------|----------------------------|-------|-------|-----|---------|
|                                  | No n (%)                   | Yes n (%) |       |     |         |
| Gender                           | Female 235 (53.9)          | 121 (63.0) | 4.52  | 0.034 |
|                                  | Male 201 (46.1)            | 71 (37.0)  | 1.38  | 0.241 |
| Educational level                | ≤Primary 336 (77.1)        | 156 (81.2) | 2.42  | 0.299 |
|                                  | ≥Secondary 100 (22.9)      | 36 (18.8)  |       |       |
| Age (years)                      | <65 122 (28.1)             | 44 (22.9)  | 0.70  | 0.402 |
|                                  | ≥65 312 (71.9)             | 148 (77.1) |       |       |
| Duration of diabetes (years)     | <10 217 (53.2)             | 90 (49.5)  | 0.42  | 0.515 |
|                                  | >10 191 (46.8)             | 92 (50.5)  |       |       |
| Smoking habit                    | Never or formerly 322 (73.9) | 137 (71.4) |       |       |
|                                  | Current users 114 (26.1)   | 55 (28.6)  |       |       |
| Exercise                         | Often (ie, regular) 240 (55.0) | 89 (46.4)  | 4.04  | 0.045 |
|                                  | Not often (ie, irregular) 196 (45.0) | 103 (53.6) |       |       |
| MNSI (n=612)*                    | ≤2 208 (48.8)              | 68 (36.6)  | 7.87  | 0.005 |
|                                  | >2 218 (51.2)              | 118 (63.4) |       |       |
| ABI (n=616)*                     | ≥0.9 387 (90.6)            | 147 (77.8) | 18.76 | <0.001 |
|                                  | <0.9 40 (9.4)              | 42 (22.2)  |       |       |
| Systolic blood pressure (n=623)* | ≤130 mm Hg 141 (32.6)      | 51 (26.7)  | 2.19  | 0.139 |
|                                  | >130 mm Hg 291 (67.4)      | 140 (73.3) |       |       |
| Diastolic blood pressure (n=623)*| ≤85 mm Hg 339 (78.5)       | 139 (72.8) | 4.21  | 0.121 |
|                                  | >85 mm Hg 93 (21.5)        | 52 (27.2)  |       |       |
| Waist circumference (cm)† (n=614)*| Normal 113 (26.5)          | 53 (28.3)  | 0.28  | 0.869 |
|                                  | Abnormal 314 (73.5)        | 134 (71.7) |       |       |
| HbA1C (%) (n=457)*               | ≤7.0 125 (38.8)            | 50 (37.0)  | 0.13  | 0.721 |
|                                  | >7.0 197 (61.2)            | 85 (63.0)  |       |       |
| Fasting blood glucose (n=499)*   | ≤126 mg/dL 121 (35.4)      | 61 (38.9)  | 0.56  | 0.454 |
|                                  | >126 mg/dL 221 (64.6)      | 96 (61.1)  |       |       |
| Total cholesterol (n=411)*       | ≤200 mg/dL 183 (64.7)      | 86 (67.2)  | 0.25  | 0.618 |
|                                  | >200 mg/dL 100 (35.3)      | 42 (32.8)  |       |       |
| Triglyceride (n=437)*            | ≤150 mg/dL 192 (63.4)      | 70 (52.2)  | 4.79  | 0.029 |
|                                  | >150 mg/dL 111 (36.6)      | 64 (47.8)  |       |       |

ABI, ankle brachial index; HbA1C, glycohaemoglobin; MNSI, Michigan neuropathy screening index; *Missing data.
†Normal: male ≤90 cm, female ≤80 cm; abnormal: male >90 cm, female >80 cm.
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**Table 2** Logistic regression of factors associated with painful diabetic neuropathy

| Variables                          | B    | SE   | OR   | p Value | 95% CI        |
|------------------------------------|------|------|------|---------|---------------|
| Ankle brachial pressure index      |      |      |      |         |               |
| <0.9                               | 1.244| 0.304| 3.40 | <0.001  | 1.9 to 6.2    |
| ≥0.9*                              |      |      |      |         |               |
| Michigan neuropathy screening index|      |      |      |         |               |
| >2                                 | 0.524| 0.226| 1.69 | 0.021   | 1.0 to 2.6    |
| ≤2*                               |      |      |      |         |               |
| Gender                             |      |      |      |         |               |
| Female*                            | 0.521| 0.228| 1.68 | 0.022   | 1.1 to 2.4    |
| Male                               |      |      |      |         |               |
| Triglyceride (mg/dL)               |      |      |      |         |               |
| >150                               | 0.476| 0.226| 1.61 | 0.036   | 1.0 to 2.4    |
| ≤150*                              |      |      |      |         |               |
| Exercise                           |      |      |      |         |               |
| Irregular*                         | 0.375| 0.223| 1.45 | 0.093   | 0.9 to 2.3    |
| Regular*                           |      |      |      |         |               |

Dependent variables: painful diabetic neuropathy (1=yes; 0=no). *Reference group.

**DISCUSSION**

According to the literature, only a few researchers have explored the prevalence of PDN, its associated factors, patient discomfort and self-relief behaviours among residents with diabetes in rural Taiwan. Furthermore, nurse-led health promotion programmes for preventing foot ulceration through a multidisciplinary approach are limited. The nurse-led health promotion programme in this study included collaboration with the Bureau of Health, public health nurses in 18 districts of Chiayi County and physicians in the local hospital and faculties in the nursing school. Although random sampling was not performed, analysis of a large rural sample yielded findings that were sufficiently reliable to assist the development of a nursing intervention in primary healthcare for early detection of PDN and prevention of foot ulceration. Two important findings related to the association between PDN and associated factors. (1) Several factors were modifiable, including abnormal values of ankle brachial pressure, Michigan neuropathy and TG levels. (2) Little attention to, or treatment of, patient discomfort was provided by primary healthcare workers, despite its high prevalence.

The prevalence of PDN in this study (31%) seems to be higher than that reported in other countries (14% in Belgium, 17 10–20% in the USA,15 32 and 16.2% in the UK).33 This disparity might be due to variations in the measurements used, duration of diabetes and the sample size. We hypothesised that the raised prevalence of PDN in this study population might have been due to the increased elderly population and prevalence of diabetes in Taiwan. Participants with PDN in this study were more likely to be women, have abnormal MNSI scores, ABI, TG levels and less likely to take part in exercise. After controlling for potential confounders, these four predictors for PDN (ie, ABI, MNSI scores, gender and TG levels) were similar to those previously reported.34–36 For instance, 71% of participants with central obesity and hypertriglyceridaemia in our study had PDN, which was consistent with the study by Smith and Singleton,24 in which three or more abnormal risk factors, obesity and hypertriglyceridaemia significantly increased the risk for DPN. In addition, Smith and Singleton22 also found that obesity and hypertriglyceridaemia were related to the loss of small unmyelinated axons, whereas glycaemic control (ie, HbA1c) was related to the loss of large myelinated fibre.

The TG levels, gender, and the early signs of preclinical DPN measured with ABI (peripheral vasculopathy) and MNSI scores (peripheral neuropathy) were found to be significant factors for PDN in this study. However, it was difficult to compare our findings with those of other studies because investigations into associated risk factors for PDN are limited. According to our understanding of the pathophysiology, PDN is primarily attributable to metabolic and microvascular alterations and affects small or large sensory fibres, leading to direct abnormalities in the somatosensory system. As a result, any change in

**Table 3** Reported discomfort with painful diabetic neuropathy (n=192)

| Feelings of most discomfort           | n (%) |
|---------------------------------------|-------|
| Pricking, stabbing, tingling, numbness, stinging | 61 (31.8) |
| Dry and painful                       | 52 (27.1) |
| Burning pain                          | 37 (19.3) |
| Inexplicable dullness…excruating      | 28 (14.6) |
| My legs do not belong to me…          | 14 (7.3) |

**Areas of most discomfort**

- One or both bases or dorsal areas or toes of the feet | 173 (90.1) |
- Lower extremities…below knee | 19 (9.9) |

**Most discomfort felt**

- During sleeping and worse at night | 76 (39.6) |
- Anytime or all day long | 73 (38.0) |
- During walking | 27 (14.1) |
- When waking up in the morning | 12 (6.3) |
- During cold days | 4 (2.1) |
Peripheral vasculopathy or peripheral neuropathy is postulated to be theoretically associated with the development of PDN. According to the responses obtained from this study, most participants with PDN received little attention or treatment for their discomfort from healthcare providers. These results were similar to other studies in which only 38.6% of French patients and 28% of patients in Belgium received appropriate treatment for their neuropathic pain. More importantly, participants in our study even reported that they engaged in potentially harmful self-relief behaviours for PDN. These risky behaviours included receiving acupuncture, using hot water and kicking their own weakened legs in an effort to reduce the discomfort. These behaviours might result in fatal complications, such as diabetic foot ulceration. Such behaviours need to be considered given that diabetes is the most common cause of death in the southwestern coastal region, Chiayi County, Taiwan.3

As in other studies, PDN was characterised as feelings of prickling, stabbing, tingling, numbness, stinging, burning pain and inexplicable dullness and excruciating pain around the base or dorsal areas of the feet, which were present throughout the day, at night or when sleeping. Although we did not explore the quality of life in those affected by PDN in greater detail, about one-third of participants with PDN had discomfort during their illness. Researchers have indicated that PDN can lead to sleep disturbance, anxiety, depression and significantly affects the overall health-related quality of life.39 40 Therefore, it is important for primary healthcare providers to establish a referral system, especially for patients with PDN in remote areas and provide them with appropriate pharmacological or non-pharmacological treatments designed to achieve a certain degree of pain relief.

Limitations
Although a large sample of participants was recruited and we employed some valid and reliable measures, nevertheless, the following study limitations should be considered: (1) missing data might have led to insignificant results for FBG, HbA1C and TG, primarily retrieved from computer records at the district health centre, as risk factors for PDN; (2) participants recruited from only one county might limit the generalisability of study findings; (3) self-reports of personal health-related behaviours (eg, frequency of exercise and cigarette smoking) might be under-reported owing to recall bias associated with ageing or comorbidity of some chronic diseases. In addition, this study does not classify former smokers into the user group; this result might reduce the effects of smoking on PDN and (4) PDN was identified through a subjective question, although the selection criteria excluded various feet problems. These results might have produced misclassification of subjects with PDN.

Given the limitations of this study, future studies should involve a data monitoring protocol during the study period and a more complete dataset, especially for glycaemic control or metabolic features.

CONCLUSION
Despite some limitations, we demonstrated associations among abnormal ABI, MNSI, TG levels and PDN in rural areas. Moreover, a relatively high prevalence of PDN was found in this study. PDN was characterised by feelings of discomfort such as prickling, stinging or burning pain, inexplicable dullness and excruciating pain in the lower limbs. Moreover, the participants in this study were older, had PDN, lived in rural areas and did not receive adequate attention or appropriate treatment from healthcare providers. To enable the early
identification of high-risk groups with PDN, especially in an elderly population, future research needs to include routine screenings of MNSI, ABI, glycaemic control, metabolic indicators and pain assessments during the annual check-up programmes. Additionally, the development and evaluation of self-relief behaviours to halt or reverse the progression of PDN need to be initiated and evaluated.

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Contributors
S-WJ and MYC: setting up and designing the study, data analysis, development of the discussion section and editing of the final draft for publication. W-NC and M-SL: setting up the study and data collection. RDB: development of the discussion section and editing of the final draft. All authors read and approved the final manuscript.

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Competing interests
None declared.

Patient consent
Obtained.

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