Prevalence of peripheral neuropathy and its impact on activities of daily living in people with type 2 diabetes mellitus

Abstract

Myanmar has one of the highest rates of diabetes in southeast Asia. This study aimed to determine prevalence and background characteristics of diabetic peripheral neuropathy and neuropathic pain, and their impact on the functioning of hands and feet, activities of daily living in people with type 2 diabetes mellitus. A total of 975 participants (age: 54.90 ± 11.24 years; duration of diabetes: 5.42 ± 5.87 years) attending the outpatient clinics of four hospitals in Myanmar were interviewed using questionnaires about pain and difficulties daily activities in the local language. The participants also underwent tests of physical functioning of both hands and feet. There were high prevalence rate of neuropathy (33.7%) and neuropathic pain (59.5%) with increasing risk in old age, longer duration of diabetes, and history of smoking. The common difficulties in daily activities were sleeping, climbing stairs, walking, and work or chores. Participants with diabetic neuropathic pain experienced more difficulties in specific activities using upper and lower extremities than did those without. Healthcare service in Myanmar should be focused on diabetic peripheral neuropathy which can lead to further disabilities.

Key Words: activities of daily living, diabetic peripheral neuropathic pain, diabetic peripheral neuropathy, Myanmar, nursing research, prevalence

1 | INTRODUCTION

The World Health Organization (WHO) estimated that the global prevalence of diabetes was 9% in 2014. The prevalence of diabetes has been increasing continuously at a faster rate in low- and middle-income countries (Shaw, Sicree, & Zimmet, 2010; WHO, 2016). Moreover, nearly half of the non-communicable disease (NCD) deaths occur in low- and middle-income countries (WHO, 2014). There was also an increasing trend of diabetes prevalence in Myanmar according to an NCD risk factor survey in 2009 (WHO, 2011), and the estimated age-standardized prevalence of diabetes (≥ 18 years) was 7.1% in Myanmar (≤ 8% of men and 8% of women). A national survey on the prevalence of diabetes in 2016 indicated that the overall prevalence according to the WHO definition was 10.5%, 9.1% in men and 11.8% in women, in Myanmar (Latt, 2016) indicating an increasing prevalence in Myanmar.

1.1 | Literature review

Diabetes has many complications that lead to decreased functioning in daily life because of the life-long nature of the disease. There were 1.5 million deaths and 89 million disability-adjusted life years due to diabetes and diabetes-related complications in 2012 (WHO, 2014). Among the diabetes-related complications, diabetic peripheral neuropathy (DPN) results in symptoms such as decreased sensation or weakness, particularly in the feet and hands, with or without diabetic peripheral neuropathic pain (DPNP). The duration of diabetes in people with DPN and DPNP ranges from 8 to 10 years (Jambart et al., 2011; Lazo Mde et al., 2014; Ogurtsova et al., 2017), and the prevalence of DPN in people with diabetes ranges from approximately 30% to 60% (Gill, Yadav, Ramesh, & Bhatia, 2014; Lazo Mde et al., 2014; Sadosky, Hopper, & Parsons, 2014). DPN and DPNP are more common in people with type 2 diabetes mellitus (T2DM) than in those with type 1 diabetes (Jaiswal et al., 2017; Lazo Mde et al., 2014). Moreover, DPN is underdiagnosed because of its asymptomatic nature, and unrecognized DPNP as a serious complication (Malik et al., 2017; Pop-Busui et al., 2017; Tanenberg, 2016).

Not only are diabetes and DPN underdiagnosed, but they may also affect the quality of life (QOL) and activities of daily living (ADL). People with diabetes suffer not only from diabetes but also from anxiety, unmet needs regarding healthcare, and the difficulties of diabetes self-management (Papaspurou et al., 2015). Studies have found that DPN and DPNP affect ADL, including exercises, working, sleeping, and walking (Dobrota et al., 2014; Kim, Jeong, Mok, Kim, & Lee, 2015; Malik et al., 2017). Diabetes is a lifelong disease, and accessibility of healthcare for those with diabetes is a critical issue in this era of increased prevalence. Therefore, primary prevention for other complications and disabilities associated with diabetes becomes critical issue.

Notably, most studies in Myanmar have focused only on the prevention and prevalence of diabetes; studies focusing on DPN, a common complication of diabetes, are rare (Almuhannadi, Ponirakis, Khan & Malik, 2018). DPN is a common cause of disability and decreased QOL in people with diabetes. Therefore, a study focusing on DPN and DPNP is warranted.

1.2 | Study Aims

The purpose of this study was to identify the prevalence of DPN and DPNP, their impacts on hand and foot function, and ADL in people with T2DM and investigate the background characteristics of those with or without neuropathy and the different levels of pain with increased severity of DPN in Myanmar.

2 | METHODS

2.1 | Study Design and Setting

This was a descriptive, cross-sectional study. Participants with T2DM who visited the outpatient diabetic clinics at the four hospitals, i.e., Yangon General Hospital, North-Okkalapa General Hospital, East Yangon General Hospital, and West Yangon General Hospital, in Myanmar were invited to participate in the study.

2.2 | Sample

The sample size (n = 975) was calculated with the formula described by Kelsey et al. (1996), which is known as the most appropriate method in epidemiological studies to estimate the sample size, using the estimated prevalence rate, with $\alpha = 0.05$, power = 0.8, and adding 20% of the sample to cover the refusal rate.

People aged over 25 years who had already been diagnosed with T2DM and were receiving anti-glycemic treatment were included in this study. People with neuropathy and neuropathic pain not due to diabetes and those with severe illness, mental illness, or alcoholism were excluded.

An accurate tally of the numbers of people who visited public hospital clinics in Myanmar could not be obtained. Therefore, based on the numbers of people in the previous year, every 5th person who visited the clinics was invited to participate in this study. Those who had already participated in this study were excluded during their repeat follow-up visits.

A total of 1965 people visited the clinics during the data collection period; 1050 were invited to participate in the study, but 20 refused to participate. A total of 55 people with type 1 diabetes, a history of stroke, alcohol-dependent syndrome, antipsychotic treatment, or anti-tuberculosis treatment were excluded according to the inclusion and exclusion criteria. Finally, 975 people who met the inclusion criteria were included.

2.3 | Data Collection

People with T2DM who visited the diabetic clinics of hospitals and met the inclusion criteria were included in this study after obtaining informed consent. Demographic and health history information was collected at the start of the interview which were held in the outpatient diabetic clinics of hospitals.

Interviewing was performed to obtain self-reports of the impact of pain on ADL using the Patient Neurotoxicity Questionnaire (PNQ), and a visual analog scale (VAS; 0–100) in

Myanmar languages. The questionnaires were independently tested for reliability via back-translation by two translators following the process of valid questionnaire translation (Su & Parham, 2002). The terminology used in the questionnaires was corrected by consulting the experts in the pain clinic of Yangon General Hospital to ensure relevancy with respect to culture and usage. The PNQ is an instrument originally developed to assess chemotherapy-induced peripheral neuropathy in people (Shimozuma et al., 2009). It is a self-reported questionnaire to evaluate the symptoms of people and their ability to perform ADL, and it has a high level of internal consistency (Cronbach's alpha = 0.719) and permission was given for both the translation and use of the questionnaire. The VAS is commonly used in pain research and is available in the public domain (Burckhardt & Jones, 2003).

Physical examinations were performed after the interviews. Hand grip, pinch strength, and the Timed Up and Go Test (TUG) were used to evaluate the physical functioning. After explaining the procedure of the TUG, the participant had to sit on a standard high armed-chair (seat, 46 cm; arm, 67 cm in height), stand up, and walk 3 m as fast as they could; and return to the chair and sit down again. The examiner recorded the total duration from the start and finish sitting position using a stopwatch. The TUG can be used to predict the fall risk with high accuracy in the people with DPN (Jernigan, Pohl, Mahnken, & Kluding, 2012). Hand grip (both hands) in kilograms (kg) was measured alternately and twice in each hand to ensure a rest time between squeezing a hand dynamometer (TTM Original Dynamometer 100 kg, Tsutsumi Seisakusho, Co. Ltd., Chiba, Japan). Finger pinch force was measured for both hands after demonstration of the procedure to the subjects using a pinch gauge (B&L Engineering®, Santa Ana, CA, USA).

Furthermore, touch sensation of the hands and feet was measured using the 10-g Semmes-Weinstein Monofilament (SWM) test at the tips of the index and ring fingers of both hands and four areas of the foot (plantar surface of the distal hallux and the first, third, and fifth metatarsal

heads) using the Touch-Test^{TM} Sensory Evaluator 5 Pieces Hand Kit (North Coast Medical Inc., Gilroy, CA, USA) (Baraz S., 2014).

2.4 | Operational Definition of DPN and DPNP

Participants were classified into three groups as follows: noDPN, people without symptoms and sensory loss; DPN, those with some degree of sensory loss but no pain; and DPNP, those with pain and sensory loss.

Symptoms were defined as the symptoms of paresthesia (numbness, tingling, or both). Sensory loss was defined as decreased sensation in one area in both feet. According to the SWM test, normal sensation thresholds were 3.61 in the hand and 4.31 in the foot (Kamei et al., 2005). Decreased sensation was defined as reported touch sensation above the normal sensation threshold. The presence of pain was determined using a VAS (0–100) score of 5–100 (Hawker, Mian, Kendzerska, & French, 2011).

The severity of DPN was defined using the well-known touch sensation filament size in the SWM test. According to the manual of the Touch-Test^{TM} Sensory Evaluator 5 Piece Hand Kit, the severity of DPN was defined by the size of the filaments: 4.31 in the hand and 4.56 in the foot as diminished protective sensation (DPN-1); 4.56 in the hand as loss of protective sensation (DPN-2); 6.65 as deep pressure sensation only (DPN-3); no response to SWM (DPN-4); and ulcer (DPN-5).

2.5 | Data Analysis

Data analysis was conducted using SPSS version 23. A logistic regression model was used to examine the effects of background characteristics. Manny Whitney *U* test was done to compare the differences in severity of DPN in DPN and DPNP. Furthermore, differences in pain intensity among people with different severities of DPN (DPN 1–5) and the impacts of DPN (people with noDPN, DPN, and DPNP) on physical functions were analyzed using the Kruskal-

Wallis *H* test. The Bonferroni correction was applied after analyzing the relationships with difficulties in each component of ADL by Fisher's exact test (McDonald, 2014).

2.6 | Ethical Considerations

The researchers obtained consent after explaining the purpose, procedure, and anonymity measures of the study to the participants. The study was approved by the Nursing Science Ethical Review Committee, Graduate School of Health Sciences, Okayama University, Japan (approval number, D16-05), University of Nursing, Yangon, and Department of Medical Research, Myanmar (approval number, Ethics/DMR/2017 /049).

3 | RESULTS

3.1 | Characteristics of Participants

This study included 975 participants, 215 males (22.1%) and 760 females (77.9%). Although the majority of participants (n = 759, 77.8%) were Burmese**,** participants in other ethnic groups were also represented in this study. Table 1 describes the characteristics of all participants in this study: age, 54.90 ± 11.24 years; duration of diabetes, 5.42 ± 5.87 years; body mass index (BMI), 25.46 ± 5.02 kg/m^2; duration of oral hypoglycemic treatment, 4.99 ± 5.53 years; TUG, 7.36 ± 3.56 seconds; hand grip, 20 ±7.27 kg; finger pinch force, 10 ± 3.86 lbs; and VAS, 14 ± 28.76.

3.2 | Prevalence of DPN and DPNP

In this study, 33.7% (n = 329) and 59.5% (n = 580) of the participants were found to have DPN and DPNP, respectively. The overall prevalence rate of DPN and DPNP was 93.2% (Table 1). Although a family history of diabetes, BMI, and the number of previous hospitalizations were similar in the three groups, people with DPNP had the longest duration of diabetes and taking oral hypoglycemic drugs. More than half of those with DPNP were using pain relief medication (50.3%) or other pain relief techniques (54.1%). Hot topical application was the most common

method of pain relief. Most participants (57.9%), including the vast majority of those with DPNP, had abnormal sensation (Table 1).

3.3 | Background Characteristics of DPN

Logistic regression was used to evaluate the effects of age, sex, BMI, a family history of diabetes, duration of diabetes, type of treatment, previous hospitalization, smoking, drinking, other complications of diabetes, and other comorbidities on the risk of developing DPN. Before the logistic regression analysis, chi-squared cross-tabulation was performed to verify significant relationships between variables. Three logistic models were assessed to determine the appropriate model for logistic regression analysis (Table 2). We found that model (3) was the significant logistic regression model, with χ^2 (24) = 56.731 and $P < 0.000$; Nagelkerke R^2 was 14.5%, with classification accuracy of 93.2% for DPN.

Compared with diabetes for less than 6 months, a longer duration of diabetes was associated with a higher prevalence of DPN (2.8 times higher in people with diabetes for 10–15 years and 3.3 times higher in people with diabetes for over 15 years), although logistic regression analysis revealed no significant differences (Table 3).

The odds ratio for people who had already quit smoking was 5.5 times that for those who had never smoked. Drinking was not associated with an increased risk of DPN in the analysis with equal numbers of drinking participants in each group, although there was a high ratio in the selected model (Table 3).

Age was also a significant risk factor for DPN, with 3–4 times higher risk in elderly people than in those younger than 40 years of age. Participants aged 50-59 years had the highest risk of DPN, probably because this group had the highest number of participants in this study. After randomly selecting equal numbers for each age group, the risk of DPN was highest (3 times) in the oldest age group (≥ 70 years), with a 2-fold higher risk in the 40–49 years of age group and a 2.5-fold higher risk in the 50–59 and 60–69 years of age groups than in the under 40

years of age group. Although both longer duration of diabetes and older age increased the risk for DPN, no significant association was observed between the duration of diabetes and age.

3.4 | Severity of DPN and Pain

There was no significant difference in DPN severity between the DPN and DPNP group according to the Mann-Whitney U test (U = 98354.5, z = 0.84, P = 0.401). In people with DPNP, differences in pain intensity were identified across the severities of DPN (DPN 1-5) using the Kruskal–Wallis H test. There was no significant difference in VAS pain scale scores between people with different severities of DPN in the combined groups (DPN and DPNP), (H [4] = 9.13, P = 0.058) and the DPNP group, (H [4] = 4.46, P = 0.326). Figure 1 shows the differences in pain intensity across DPN severities in the combined and DPNP group.

3.5 | Difficulties in physical function and activities of daily living

The Kruskal-Wallis test was used to evaluate differences in physical functioning of the hand and foot and ADL among those with noDPN, DPN, and DPNP. Hand grip and pinch strengths were calculated using the dominant hands of the participants. TUG duration and hand grip and pinch strengths were significantly different among the three groups. Those with DPNP had the longest TUG duration and the weakest strengths of both hand grip and pinch (Table 4).

TUG duration was significantly different among the three groups (H [2] = 23.903, P = 0.000), with a mean rank score of 399.24 for people with noDPN, 443.51 for those with DPN, and 523.34 for those with DPNP. Pairwise comparisons showed significant differences in TUG duration between people with DPNP and those with noDPN (P = 0.002, r = −0.11) or those with DPN (P = 0.000, r = −0.13).

Hand grip strength was also significantly different among the three groups (H [2] = 34.292, P = 0.000). Pairwise comparisons were performed to ascertain differences between groups. People with DPNP (mean rank = 444.46) had significantly different hand grip strengths

compared with those with noDPN (mean rank = 550.14; $P = 0.012$, $r = 0.09$) or those with DPN (mean rank = 552.29; $P = 0.000$, $r = 0.18$).

Pinch strength was also significantly different among the three groups (H [2] = 24.576, $P = 0.000$). Pairwise comparisons showed a significant difference in pinch strength between people with DPNP (mean rank = 451.27) and those with DPN (mean rank = 543.20; $P = 0.000$, $r = 0.15$).

The Kruskal-Wallis H test revealed significant differences in sensory (H [2] = 205.823, $P = 0.000$) and motor (H [2] = 141.287, $P = 0.000$) scores of the PNQ among the three groups. Pairwise comparisons found significant differences between those with DPNP (mean ranks: 586.51 and 572.12 for sensory and motor, respectively) and those with noDPN (mean ranks: 233 and 332.83 for sensory and motor, respectively) or those with DPN (mean ranks: 365.50 and 377.38 for sensory and motor, respectively).

The numbers of difficulties in ADL were also significantly different among the three groups (H [2] = 168.860, $P = 0.00$). People with DPNP (mean rank = 577.23) had the highest number of difficulties in ADL, and pairwise comparison tests revealed significant differences between people with DPNP and those with noDPN or DPN (mean rank with noDPN = 255.26; mean rank with DPN = 377.38). Most had difficulties in sleeping (20.6%), climbing stairs (24.5%), walking (21.3%), and work or chores (14.4%). The Fisher's exact test with Bonferroni correction was conducted after the analysis of the relationships with difficulties in each ADL, with a significant level at $P < 0.017$ (McDonald, 2014). There were significant differences in specific ADL (putting buttons, using a knife, using a fork, using a spoon, using other eating utensils, opening doors, sleeping, climbing stairs, walking, working, or chores) among the three groups (Table 5).

4 | DISCUSSION

The majority of the participants were found to have DPN in this study, with a high overall prevalence of 93.2%. The higher prevalence of DPN in Myanmar in this study than in other countries in previous studies (Gill et al., 2014; Kim et al., 2015; Lazo Mde et al., 2014) may be due to underdiagnosis and poor control of diabetes in Myanmar (WHO, 2011). This study is the first survey focusing systematically on the occurrence of peripheral neuropathic pain symptoms in people with diabetes in Myanmar. Taking anti-hyperglycemic treatment has been considered one of the reasons for the high prevalence of DPN (Beulens, Hart, Kuijs, Kooijman-Buiting, & Rutten, 2015).

Our findings were consistent with previous studies that have identified older age and longer duration of diabetes as risk factors for developing DPN (Jaiswal et al., 2017; Jambart et al., 2011; Lazo Med et al., 2014). Moreover, our study highlighted that older age and duration of diabetes were independent risk factors for developing DPN. Although these are both unmodifiable and unavoidable factors in those with diabetes, the risk of developing DPN was not magnified.

Additionally, previous studies showed that DPN was significantly associated with smoking (Jaiswal et al., 2017; Katulanda et al., 2012). This study showed that the prevalence of DPN was likely higher in people who quit smoking. Although these studies reported an increased risk of DPN in those who smoke, the effect of smoking cessation on DPN is not well understood. Future studies should focus on the effects of smoking, including duration and smoking cessation, on the risk of developing DPN.

Abbott et. (2011) found that there was no relationship between neuropathy severity and painful symptoms. Pain intensity in participants with DPNP was not significantly different across levels of DPN severity in the current study. As such, our findings were consistent with Abbott

et al. (2011). Health care practitioners should separately assess the severity of neuropathy using both objective physical examination, and subjective measurements of pain.

In a previous study, people with overt neuropathy had a longer TUG duration than those without overt neuropathy (Timar et al., 2016). People with DPNP had the highest TUG duration in this study, suggesting that they have a higher risk of falls than others.

The severity of neuropathy also affects functional hand movement in patients with DPN and other types of neuropathy (Adams et al., 2015; Yang et al., 2015). This study did not investigate the association between the severity of DPN and functional hand movement. Regardless of the severity of DPN, participants who were suffering DPN with pain exhibited the greatest functional hand weakness.

A previous study also found that the physical strength of the hand was associated with independence in ADL (Bae et al., 2015). These findings are also relevant showing that those with DPNP who have the greatest functional hand weakness also have difficulties in performing hand-based tasks (putting buttons, using eating utensils, opening doors, and work or chore).

Previous studies found that people with DPN had difficulties in sleeping, balance and walking, and work and chores (Brod, Pohlman, Blum, Ramasamy, & Carson, 2015; Malik et al., 2017). Some investigators demonstrated that problems with sleeping and walking were more prominent in people with painful DPN than in those with pain but without neuropathic symptoms (Bouhassira, Letanoux, & Hartemann, 2013; Dobrota et al., 2014). The current study identified significant difficulties in putting buttons, using eating utensils, opening doors, sleeping, climbing stairs, and walking, work or chore in people with DPNP. However, the qualities of specific difficulties in daily living were not investigated in this study. Further studies should focus on the severity of difficulties of specific components of ADL in people

with DPN and DPNP. Moreover, researchers should explore better methods of providing nursing care to improve ADL in the future.

4.1 | Limitations

First, the participants did not accurately represent all ethnic groups in Myanmar. The effect of ethnicity on DPN should be identified in future studies because different beliefs, eating habits, and health practices also affect health outcomes. Second, our study involved more female than male participants. Third, only the monofilament test was used to diagnose DPN. Fourth, hemoglobin A1c (HbA_1C) levels were not analyzed in this study. Finally, only participants taking anti-hyperglycemic treatment were included in this study to ascertain their glycemic control because of the underdiagnosis and poor control of diabetes in Myanmar (Latt et al., 2016; WHO, 2011).

5 | CONCLUSION

In conclusion, this study highlighted the high prevalence of DPN, ADL difficulties, and the background characteristics of people with DPN in Myanmar. The background characteristics of people with DPN in the current study were similar to those identified in other countries and studies. We suggest that healthcare services and professionals focus on the high-risk group for DPN, with the aim of preventing further complications. The findings highlight the difficulties those with DPN can have with specific ADLs, especially when activities require the use of the extremities. These findings will help develop future studies to improve QOL, ADL, and healthcare for people with DPN.

AUTHORS CONTRIBUTIONS

Study design: M.M.T.M.W., K.F.

Data collection: M.M.T.M.W., H.H.N., K.Z L.

Data analysis: M.M.T.M.W., K.F., Y.H.

Manuscript writing and revisions for important intellectual content: M.M.T.M.W., K.F.

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