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# A higher incidence of diabetic peripheral neuropathy may be associated with decreased sleep and increased depression in older adults

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## ABSTRACT

**Aim:** Diabetes mellitus (DM) tends to increase with aging. Nearly half of the patients with DM develop neuropathy (DPN). Despite its high burden and morbidity, the conditions that DPN may be associated with have not been adequately studied in older adults. We aimed to identify sleep duration and comprehensive geriatric assessment components that may be associated with DPN.

**Material and Method:** This is a cross-sectional retrospective study. DPN diagnosed with a medical history, neurologic examination, and electromyography (EMG). 125 diabetic older patients were included. All comprehensive geriatric assessment tests and questions about sleep quality and time were performed. We divided the patients into two groups those without neuropathy and with neuropathy and compared them.

**Results:** The median age of 125 patients was 72 (min-max; 64-94). 58.8% of them were women. The percentage of married people and living with their spouse and slept for 6 hours or more had a lower percentage in the DPN group. Polypharmacy and the percentage of heart failure were significantly higher in the DPN group. Lawton-Brody score, which shows instrumental daily living activities (IADL) and geriatric depression score (GDS) was higher in the DPN group. In logistic regression, we found that depression scores were higher and sleep duration was shorter in the DPN group (respectively, odd ratio:265 p:.012; odd ratio:.1.917 p:.045)

**Conclusions:** DPN in older adults may affect the functionality and be associated with fewer sleep hours and depression. Not only blood glucose regulation but also other factors such as sleep duration and depressed mood may be associated with DPN in older adults.

**Keywords:** Diabetic neuropathy, comprehensive geriatric assessment, older adults, sleep duration, depression

## INTRODUCTION

The incidence of diabetes mellitus (DM), particularly type 2 DM, tends to increase with age. Moreover, it is estimated that the prevalence of DM in older adults will be around 20% in the future (1). Diabetic peripheral neuropathy (DPN) has been defined as a length-dependent, symmetrical sensorimotor polyneuropathy linked to metabolic and microvascular changes resulting from chronic high blood glucose exposure from DM, as well as cardiovascular changes (2). Complications of neuropathy develop in approximately half of the patients followed for DM (3). As a result, it is predicted that this painful condition will affect approximately 10% of older adults in the 2030s (4).

The etiology of diabetic neuropathy has not been fully elucidated, but the possible underlying cause is hyperglycemia and microangiopathy. The most common form is distal symmetric sensorimotor polyneuropathy, but most body systems can be effected through the involvement of autonomic nerves (5).

DPN causes not only pain but also loss of activity and decreased quality of life. In older adults, DPN causes

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decreased vibration, pressure, and sensory losses. This causes balance and coordination disorders in walking. As a result, older adults tend to lose muscle strength and fall (6,7). In addition, it can disrupt sleep and mood, decrease quality of life, and negatively affect their activities of daily living (ADLs). Geriatric syndromes can be defined as common health problems that result from the disruption of more than one system in older adults. These syndromes can be identified by comprehensive geriatric assessments (CGA). It is possible to say that DPN is more common in older adults with the increase in years of exposure to high blood glucose. Diabetes treatment in older adults is more difficult due to cognitive and physical problems. The presence of geriatric syndromes is thought to complicate adherence to diet and treatment for diabetes. Therefore, evaluating the relationship between geriatric syndromes and diabetes-related complications like DPN is important. The tests used in CGA evaluate the basic and instrumental daily activities, mental status, and nutritional status of older adults. DPN can cause walking difficulties, depression that may be associated with chronic disease, and pain. This situation may cause deterioration in the general mental and physical activities of the older adults evaluated by CGA(5,8,9).

Despite its high health burden and morbidity, the conditions with which DPN may be associated have not been adequately researched in older adults. At present, a few studies have investigated associations between diabetic neuropathy and sleep and comprehensive geriatric assessments in older adults. DPN was found in 28.2% of older diabetics. They found that DPN was associated with lower Mini-Mental Status Examination, Activities of Daily Living, Instrumental Activities of Daily Living, and higher Mini Geriatric Depression Scales (8,10,11). Older adults are excluded from most studies of complications of diabetes. Therefore, there is a need for more studies investigating interactions in older adults.

Thus, this study aimed to identify sleep duration and comprehensive geriatric assessment components that may be associated with diabetic peripheral neuropathy in older adults.

## MATERIAL AND METHOD

The study was approved by the Clinical Resarches Ethics Committee of the Ankara University Medical Faculty (Date: 13.08.2018, Decision No: 13-878-18). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Participants

125 patients admitted to geriatrics clinics were included in this cross-sectional, retrospective study. Individuals diagnosed with diabetes-related neuropathy based on medical history and peripheral neurologic examination and with electromyography (EMG) findings recorded in their files were included. Persons with incomplete demographic data and comprehensive geriatric assessment records were excluded from the study. The patients' sociodemographic data are shown in **Table 1**.

**Table 1:** Demographic, comprehensive geriatric assessment and laboratory values of the participants and comparisons by group

| *Variables | Without neuropathy n=89 (71.2%) | With neuropathy n=36 (28.8%) | All n=125 (100%) | p-value |
|---|---|---|---|---|
| Sociodemographics | | | | |
| Age, median (range) | 71 (64–87) years | 73 (64–94) years | 72 (64–94) years | .260 |
| Gender, n (%) | | | | .921 |
| Female | 61 (48,8) | 25 (10.0) | 86 (58.8) | |
| Male | 28 (22.4) | 11 (8.8) | 39 (41.2) | |
| Educational status, n (%) | | | | .095 |
| <5 years | 40 (31.7) | 24 (19.0) | 64 | |
| 6–8 years | 36 (28.6) | 11 (8.7) | 47 | |
| >8 years | 13 (10.3) | 2 (1.6) | 15 | |
| Marital status, n (%) | | | | <.005 |
| Married | 47 (42.0) | 11 (9.8) | 58 (51.8) | |
| Widowed or divorced | 33 (29.5) | 21 (18.8) | 54 (48.2) | |
| Living situation, n (%) | | | | <.005 |
| Alone | 22 (19.5) | 12 (10.6) | 34 (30.1) | |
| With partner | 36 (31.9) | 11 (9.7) | 47 (41.6) | |
| With child/children | 11 (9.7) | 10 (8.8) | 21 (18.6) | |
| With somebody else | 11 (9.7) | 0 (0) | 11 (9.7) | |
| Living place, n (%) | | | | .345 |
| Nursing home | 2 (1.8) | 2 (1.8) | 4 (3.5) | |
| Private home | 79 (69.3) | 31 (27.2) | 110 (96.5) | |
| Sleep quality, n (%) | | | | .122 |
| Poor | 19 (19.2) | 13 (13.1) | 32 (32.3) | |
| Good | 50 (50.5) | 17 (17.2) | 67 (67.7) | |
| Sleep duration, n (%) | | | | <.005 |
| <6 hours | 17 (18.5) | 14 (15.2) | 31 (33.7) | |
| ≥6 hours | 46 (50) | 15 (16.3) | 61 (66.3) | |

(cont...)

**Table 1:** Demographic, comprehensive geriatric assessment and laboratory values of the participants and comparisons by group (cont...)

| *Variables | Without neuropathy n=89 (71.2%) | With neuropathy n=36 (28.8%) | All n=125 (100%) | p-value |
|---|---|---|---|---|
| Diseases | | | | |
| Hypertension, n (%) | 68 (54.0) | 31 (24.6) | 99 (78.6) | .358 |
| COPD, n (%) | 13 (10.3) | 5 (4.0) | 18 (14.3) | .873 |
| Heart failure, n (%) | 3 (2.4) | 8 (6.3) | 11 (8.7) | **<.005** |
| Dementia, n (%) | 4 (3.2) | 5 (4.0) | 9 (7.1) | .073 |
| Cerebrovascular disease, n (%) | 6 (4.8) | 4 (3.2) | 10 (7.9) | .442 |
| Hypothyroidism, n (%) | 13 (10.3) | 3(2.4) | 16 (12.7) | .318 |
| Coronary artery disease, n (%) | 19 (15.1) | 10(7.9) | 29 (23) | .490 |
| Smoking, n (%) | 19 (18.1) | 7 (6.7) | 26 (24.8) | .738 |
| Nephropathy, n (%) | 3 (2.4) | 11 (8.7) | 14 (11.1) | **<.001** |
| Retinopathy, n (%) | 6 (4.8) | 9 (7.1) | 15 (11.9) | **<.001** |
| Comprehensive geriatric assessment | | | | |
| Polypharmacy, n (%) (>5 drug use) | 27 (21.4) | 45 (35.7) | 72 (57.1) | **<.005** |
| Number of drugs mean (range) | 5 (1–9) | 6 (0–13) | 5 (0–13) | **<.005** |
| Number of falls mean (range) | 0 (0–3) | 0 (0–3) | 0 (0–3) | .865 |
| Katz ADL mean (range) | 6 (4–6) | 6 (4–6) | 6 (4–6) | .366 |
| Lawton–Brody IADL mean (range) | 8 (2–8) | 7 (2–8) | 7 (2–7) | **<.005** |
| MMSE score mean (range) | 24 (10–30) | 25 (13–29) | 24 (10–30) | .669 |
| MNA-SF score mean (range) | 13 (10–14) | 13 (10–14) | 13 (10–14) | .290 |
| GDS score mean (range) | 3 (0–8) | 4 (0–9) | 3 (0–10) | **<.005** |
| Depression score, n (%) | | | | **<.001** |
| <5 | 71 (56.3) | 17 (13.5) | 88 (69.8) | |
| ≥5 | 18 (14.3) | 20 (15.9) | 38 (30.2) | |
| Handgrip strength (kg) mean (range) | 18.5 (0–41.7) | 21.2 (5.10–39) | 19.4 (0–41.70) | .400 |
| **Laboratory values** The mean and standard deviation for the normally distributed variables and median and range for the non-normally distributed variables | | | | |
| Fasting blood glucose (mg/dL) | 131 (80–306) | 126 (86–462) | 131 (80–462) | .803 |
| Creatinine (mg/dL) | 0.81 (0.51–1.56) | 0.85 (0.55–2.76) | 0.84 (0.50–2.76) | .431 |
| GFR (ml/min/1.73 m²) | 81 (16–90) | 71.5 (16–90) | 78 (16–90) | .207 |
| Sodium (mmol/L) | 138 (127–142) | 139.5 (131–143) | 139 (127–143) | .077 |
| Potassium (mmol/L) | 4.5 (4–5.40) | 4.6 (3.50–5.10) | 4.6 (3.50–5.40) | .552 |
| Calcium (mg/dL) | 9.93±0.56 | 9.87±0.47 | 9.50±0.53 | .062 |
| Albumin (g/L) | 4.2 (3–4.70) | 4.10 (3.40–4.70) | 4.10 (3–4.70) | **<.005** |
| Total cholesterol (mg/dL) | 185.8 (122.1–375.2) | 192.8 (117.2–315.4) | 177.4 (117.2–375.2) | .963 |
| LDL (mg/dL) | 104.6 (64.3–253.3) | 107.5 (56.7–246.4) | 105.8 (56.7–253.3) | .917 |
| Alanine aminotransferase (ALT) (U/L) | 17 (9–122) | 16 (8–44) | 16 (8–122) | .754 |
| Aspartate aminotransferase (AST) (U/L) | 24 (11–88) | 18 (8–57) | 20 (8–88) | .290 |
| Sedimentation (mm/h) | 20 (4–60) | 21 (3–13) | 20 (3–60) | .466 |
| Leukocyte (WBC) (×10⁹/L) | 8.19 (3.03–13.0) | 7.5(3.97–11.30) | 7.75 (3.03–13.0) | .696 |
| Hemoglobin (Hb) (g/dL) | 13.5 (8.60–16.20) | 12.5 (10–14.20) | 13.0 (8.60–16.20) | **<.001** |
| Hematocrit (%) | 40.7 (26.5–49.0) | 38.80 (30.90–44.10) | 40.10 (26.5–49.0) | **<.005** |
| Platelet Count ×10⁹/L | 291.9±93.44 | 283.66±62.37 | 289.93±83.50 | .319 |
| HbA1c (with electrophoresis method) (%) | 7.3 (5.40–11.50) | 7.45 (5.70–17.02) | 7.40 (5.40–17.02) | .835 |
| Vitamin B12 (pg/mL) | 243 (102–1500) | 322 (151–1500) | 301 (102–1500) | .217 |
| TSH (μIU/mL) | 1.75 (0.08–72.8) | 1.57 (0.51–4.83) | 1.72 (0.08–72.80) | .348 |
| Folate (ng/mL) | 9 (4–25) | 8.2 (1.68–25) | 8.98 (1.68–25) | .176 |
| CRP (mg/L) | 3 (0.30–76) | 4.5 (0.6–210) | 3.20 (0.30–210) | .331 |
| 25-hydroxy vitamin D (μg/L) | 20.98±10.07 | 19.42±9.80 | 20.43±9.94 | .494 |

* Percentages in cells show percentages in the total. Missing values are included in the calculation of the percentages. The results of the descriptive analyses were presented in mean and standard deviation for the normally distributed variables and in median and range for the non-normally distributed variables. The frequencies of the categorical variables were expressed as (%). The percentage comparison of categorical variables was performed with the Chi-squared test. An independent t-test was used for normally distributed variables for 2 groups to compare means, and the Mann–Whitney U test was used for 2 groups for comparison of non-normally distributed continuous variables. The correlations between normally distributed numerical variables were evaluated using the Pearson test, and the non-normally distributed variables were evaluated using the Spearman test. Statistical significance was accepted as p<0.05. Values in bold are significant.

Abbreviations: COPD: chronic obstructive pulmonary disease, Katz ADL: Katz index of activities of daily living; LB-IADL: Lawton–Brody instrumental activities of daily living scale; MMSE: mini-mental state exam; MNA-SF: mini nutritional assessment-short-form; GDS: geriatric depression scale; GFR: glomerular filtration rate; TSH: thyroid-stimulating hormone; CRP: C-reactive protein.

**Comprehensive Geriatric Assessment**

Comprehensive geriatric assessment tests include the Katz Activities of Daily Living Index (Katz ADL), Lawton-Brody Instrumental Activities of Daily Living Scale (LB-IADL), Geriatric Depression Scale (15-item short form) (GDS), Mini-Mental State Examination (MMSE), and Mini Nutrition Assessment-Short Form (MNA-SF).

ADLs were assessed using the Katz ADL, which assesses bathing, dressing, going to the toilet, transfer, feeding, and continence; 0 or 1 point is given for each activity for a total score of 0–6 points (12). Instrumental ADLs were evaluated with the LB-IADL on a total scale of 0–8 points; 0 or 1 point was given for each activity. This scale evaluates using the phone, shopping, preparing meals, cleaning the house, doing laundry, using modes of transportation, being able to control finances, and being responsible for one's medications (13). Cognitive functions were examined and recorded using the MMSE test, which is valid and reliable in a Turkish setting. It grades cognitive functions in a 30-point range, with low scores indicating cognitive function impairments. (14). The nutritional status of the patients was evaluated with the MNA-SF test, in which the maximum obtainable score is 14: 0–7 points indicate malnutrition, 8–11 points indicate pre-malnutrition and 12–14 points indicate normal nutrition statuses (15). Muscle strength was assessed using an electronic hand dynamometer (GRIP-D digital handgrip dynamometer; Takei, Tokyo, Japan). The number of falls experienced by the individual during the one year preceding the test was documented by asking the patients and/or their relatives. The sleep duration of each patient was recorded as either less than 6 hours or 6 hours or more. The cut-off time of 6 hours was determined by reviewing the results of similar previously published studies (16, 17).

**Laboratory Assessment**

These values were added to the study because they were related to the general health, nutrition, and inflammatory status of the patients. Biochemical parameters were studied using spectrophotometry. C-reactive protein (CRP) levels were determined by the turbidimetric method, hormonal levels were determined by the electrochemiluminescence immunoassay (ECLIA) method, and vitamin D levels were determined using the high-performance liquid chromatography (HPLC) method.

Fasting plasma glucose (FPG) and HbA1c values were used to determine a diagnosis of DM. Blood samples were taken by venipuncture after overnight 12-h fasting. FPG was measured using the glucose oxidase method. HbA1c levels were measured in the same laboratory by HPLC. Fasting plasma glucose levels of ≥126 mg/dl and HbA1c of ≥6.5% were considered diagnostic of DM.

**Statistical Analysis**

Statistical Package for the Social Sciences (SPSS) for Windows version 24.0 (IBM SPSS Inc., Chicago, IL) was used to perform statistical analyses. The conformity of the variables to the normal distribution was examined using visual (histograms and probability graphs) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. The results of the descriptive analyses were presented as mean and standard deviation (for normally distributed variables), median, and minimum-maximum range (for non-normally distributed variables). The frequency of the categorical variables was given as a percentage (%). An independent t-test was used to compare the means of the two groups. The Mann–Whitney U test was used to compare the two groups that did not fit the normal distribution. Multivariate logistic regression analysis was performed using the Enter method with independent variables (Model 1) that were significant in univariate linear regression analysis and independent variables that could be clinically significant (Model 2). The results were evaluated within the 95% confidence interval (CI), and a p-value <0.05 was considered statistically significant.

## RESULTS

The median age of the 125 patients included in the study was 72 years (range: 64–94 years); 58.8% were women. Among the 125 patients, 89 (71.2%) had neuropathy (neuropathy group), whereas 36 (28.8%) had no neuropathy (non-neuropathy group). The number of married people was significantly lower in the neuropathy group. The percentage of those living with their spouses was lower. In the comparison of sleeping hours, those who slept for 6 hours or more had a lower percentage of neuropathy. The percentage of those with heart failure was significantly higher in the neuropathy group. The incidence of retinopathy and nephropathy was also higher in the neuropathy group. Moreover, the polypharmacy rate and the median number of drugs used were significantly higher in the neuropathy group.

The median of the Lawton–Brody score, which shows instrumental ADLs (IADLs), was found to 8(2-8) in without neuropathy group and 7(2-8) in with neuropathy group (p-value: <.005). The median geriatric depression score (GDS) was 3(0-8) in without neuropathy group and 4(0-9) in with neuropathy group (p-value: <.005). In the grouping of depression scores according to the cut-off used for depression, the percentage was found to be higher in the neuropathy group. In the comparison of laboratory results, albumin, hemoglobin, and hematocrit values were found to be significantly lower in the neuropathy group. Demographic, CGA, and laboratory values and comparisons by the group are shown in **Table 1**.

Models were used in the logistic regression analysis. DPN was taken as the independent variable. In Model 1, univariate analysis was performed with the variables found to be significant as shown by the comparisons in **Table 2**. In Model 2, factors that were found to be associated with neuropathy in previous studies were analyzed using univariate analysis. In Model 3, significant variables were analyzed in Models 1 and 2 and included in the multivariate analysis.

**Table 2.** Univariate linear and multivariate logistic regression analysis of factors associated with diabetic neuropathy

| Variable | Univariate analysis | | |
|---|---|---|---|
| | Odds ratio | p-value | 95% CI |
| Model 1 | | | |
| Heart failure | .126 | .002 | .031–.509 |
| Polypharmacy | .379 | .023 | .164–.874 |
| Sleep duration (≥ 6 h) | 2.525 | .048 | 1.010–6.315 |
| Lawton-Brody IADL | .890 | .067 | .786–1.008 |
| GDS groups (≥ 5 point) | 1.179 | .030 | 1.016–1.368 |
| Hemoglobin (Hb) | .720 | .011 | .559–929 |
| Model 2 | | | |
| Age | 1.043 | .921 | .451–2.413 |
| HbA1c | 1.042 | .684 | .852–1.277 |
| Vitamin B12 (pg/mL) | 1.004 | .382 | .987–1.009 |
| Folate (ng/mL) | .964 | .370 | .88–1.045 |
| Model 3 | | | |
| **Variable** | **Multivariate analysis** | | |
| | **Odds ratio** | **p-value** | **95% CI** |
| Heart failure | .177 | .063 | .029–1.096 |
| Hemoglobin (Hb) | .356 | .145 | .259–.569 |
| Sleep duration (<6 hours) | 1.917 | .045 | .678–5.418 |
| Polypharmacy | .428 | .119 | .147–1.244 |
| GDS groups (≥5 point) | .265 | .012 | .094–5.417 |

## DISCUSSION

To our knowledge, this is the first study in Türkiye to examine the relationship between diabetic neuropathy and CGA components in older adults. The main finding of this study is that diabetic neuropathy is a condition that may negatively affect the IADLs of older adults, and a higher incidence of diabetic neuropathy may be associated with depression and less (i.e., <6 hours a day) sleep. As a result of these analyses, we found that there may be a relationship between the geriatric depression score, sleep duration, and diabetic peripheral neuropathy in older adults. Moreover, we found that the risk of developing neuropathy increases 0.2 times when depression scores are high and 1.9 times with less than 6 hours of sleep a day.

Diabetic neuropathy is a complication that affects functionality and quality of life, especially among older adults. Previous studies have examined how complications can be prevented by DM regulation, especially in the middle-aged group. However, complications develop as an inevitable result of aging and long-term DM. We designed this study to draw attention to these inevitable results. In the current study, we observed that the rate of diabetic neuropathy was lower in married individuals; however, in some studies examining demographic data, no significant difference was found (8).

A population survey study of 33,663 people, in which demographic data but no comparisons were given, found that as the marriage rate decreased, more serious complications increased (18). This situation can be interpreted as married people being more motivated to care for their chronic illnesses, and their partners can help in their care. This interpretation is strengthened by the fact that diabetic neuropathy was less common in the married people we identified in this study.

One of the main targets of our study was sleep problems. As a result of this study, we also determined a relationship between diabetic neuropathy and sleep. The rate of diabetic neuropathy was significantly lower in those whose sleep duration was longer than 6 hours a day. In other words, we found that diabetic neuropathy was associated with decreased sleep duration. In logistic regression, less sleep was found to be significantly associated with DPN. Moreover, a systematic review of sleep problems and diabetic neuropathy found that diabetic neuropathy was more common in patients with sleep apnea-hypopnea syndrome (19). Moreover, it has been stated that diabetic neuropathy may worsen sleep quality by causing pain and nocturia (19). Furthermore, a meta-analysis showed that restless leg syndrome (related to sleep disorders) may also be associated with diabetic neuropathy (20).

A study on treatment with melatonin together with pregabalin for painful diabetic neuropathy is interesting. It has also been reported that sleep deprivation may lead to hyperalgesia and a decrease in pain thresholds, which can be attributed to variations in melatonin levels (21). Besides, it is well-known that apart from its effects on the regulation of circadian rhythms in general as well as sleep-wake rhythms, melatonin also has neuroprotective, antioxidant, anti-inflammatory, immunomodulatory, anti-nociceptive, anti-depressant, anxiolytic, locomotor activity regulator, pressure-lowering ring, and antitumor activity effects. Therefore, other studies support our hypothesis that insufficient sleep may cause neuropathy, as well as other diseases due to a lack of melatonin, which is protective, as mentioned above (21).

Regarding comorbidities, we found that the rate of heart failure was higher in the diabetic neuropathy group (the diagnosis of heart failure was confirmed by a cardiologist). Moreover, cardiovascular autonomic

neuropathy (affecting the cardiovascular system) is possible in these patients; indeed, this is one of the most common complications of diabetes.

There are several mechanisms by which clinical heart failure develops, particularly metabolic changes, such as oxidative stress-mediated by reactive oxygen species (ROS), decreased myocardial perfusion due to endothelial dysfunction, autonomic dysfunction, and impaired glucose levels caused by insulin resistance (22). Irregular neurohormonal activation, due to diabetic neuropathy, leads to many diabetes-related cardiovascular diseases. Many neuropeptides are involved in cardiac injury. For this reason, the co-occurrence of these two diseases (DM and cardiovascular disease) is common (23). In fact, in a study of 4095 DM participants without detected heart failure, at least one of nephropathy, retinopathy, and neuropathy was detected in 34.8% upon evaluation (24).

Indeed, DM is a major risk factor for heart failure. Thus, even in undiagnosed patients, heart failure should be considered. In the logistic regression analysis performed in the current study, statistical significance was lost with co-factor assets. However, the clinical risk is always present.

We also obtained interesting results regarding the relationships between comprehensive geriatric assessments and DPN, which is the main aim of our study. The polypharmacy rate was higher in the neuropathy group, and the mean number of drugs was also significantly higher in the neuropathy group.

Considering that there are complications in people with uncontrolled DM treatment, multiple diabetes medications may be useful. The most common and disturbing effect of DPN is pain. Indeed, patients with DPN may take many painkillers.

It is well known that older adults often have many comorbidities and therefore may suffer from the side effects of polypharmacy (25). In another study conducted in Türkiye, the relationship between foot ulcers, one of the worst complications of diabetic neuropathy, and polypharmacy was examined. Complaints of hypertension, ischemic heart disease, and diabetic retinopathy were found to be significantly higher in patients with diabetic foot ulcers and polypharmacy (26).

DPN is one of the main causes of low handgrip strength and falls in older adults. In addition to age and polypharmacy, diabetes-related loss of strength, sensory perception, and loss of balance and cognitive function due to peripheral neuropathy contribute to an increased risk of low handgrip strength and falls (27).

In many other studies, the incidence of falls due to loss of balance and sensory damage was higher in the neuropathy group, and neuropathy was considered one of the main causes of falls in older adults. However, no correlation between falls and DPN was found in the results we obtained, which may be due to the small number of patients in the DPN group in our study. This may also be because most participants in our study were outpatients.

The effect of DPN on functionality in older adults is commonly seen in geriatric practice. Indeed, previous studies have shown that DPN affects both quality of life and daily functions, not only in the older adults but also in the general population (28, 29). A study conducted on older adults found that DPN affects ADLs but not IADLs (8). In our study, unlike this result, we found that DPN was not associated with ADLs but could be negatively associated with IADL.

The effect of DPN on functionality may be due to both its metabolic effects and its negative effects on the mental states of patients. In addition, most people with DPN have difficulty walking transferred because it is painful. We know that walking affects many IADLs. Indeed, DPN seems likelier to affect patients' IADLs. In the logistic regression analysis, this correlation decreased in the presence of cofactors.

Depression is another common geriatric syndrome whose relationship with DPN was investigated in our study. In our study, both the mean depression scores and their grouping were found to be higher in the DPN group. Moreover, it has also been emphasized in previous studies that DPN is associated with depression (30). In all studies of complications caused by DM, it has been shown that patients with DPN are more prone to depression compared to other microvascular complications (30, 31). Given the high prevalence of depression and DPN in diabetes, it is hardly surprising that these two conditions are related. In two meta-analyses, depression was independently associated with DPN (32, 33). In addition, antidepressants are used effectively to treat depression (34). It has been determined that DPN patients with high depression screening test scores feel pain more (35).

In most of the studies mentioned above, people over the age of 65 years were not included. One of the aims of the current study was to highlight this bias. Our study showed that there are similar findings in the relationship between DPN and depression in the over-65 age group. In addition, one of the conditions independently associated with DPN is included in the analysis in Table 3.

Regarding the comparisons of the laboratory results, in the DPN group, albumin, hemoglobin, and hematocrit values were observed to be low, which (when combined) suggests possible nutritional disorders. These nutritional deficiencies may be the cause of (or contribute to)

neuropathy. Drugs (used in the treatment of DPN), absorption deficiencies, and autoimmune conditions (such as pernicious anemia) may be the cause of anemia (36, 37).

In our study, we found no significant difference (according to the MNA scores) between the groups in terms of nutritional deficiency. We also found that there was no significant difference between the groups in terms of vitamin B12, folate, and vitamin D levels, which may cause or affect neuropathy when in nutritional deficiencies. We would like to point out that we could not find a relationship between these nutrients at the end of the study, since the difference between the neuropathy groups in albumin and hemoglobin values disappeared in multivariate logistic regression analysis (Model 3).

Another remarkable result is that there was no difference in the Hba1c results between the two groups (with or without DPN). Previous studies have shown that DM patients complaining of neuropathic pain have DM for a long period and poor glycemic control(5, 38, 39).

In our study, there was no significant difference in HbA1c values between the groups. The average HbA1c percentage in the participants in our study was 7.40%. Hence, their control of DM was within good limits. Among older adults, the Hba1c value, which shows the regulation of diabetes in the previous 3 months, may not have a significant relationship with neuropathy, unlike the general adult population.

The main strength of this study is that it evaluates DPN in older adults together with a comprehensive geriatric assessment, including sleep duration and laboratory values. Additional diseases and nutritional conditions that may affect neuropathy were also included in the study. A clinical psychiatric evaluation was performed for depression. Diagnosis of DPN was made by clinical evaluation, and patients diagnosed by a neurologist were included in the study.

This study has some limitations. First, the study could not yield a causality result due to its retrospective cross-sectional structure; it only considered factors that may be related. Due to the same structure, the number heterogeneity between the groups could not be achieved. Since the study was conducted with patients who applied to a health institution due to their complaints, it cannot be said that the results fully reflected the epidemiological findings. Second, the duration of DM in each participant was not noted in the study, despite DM duration being closely related to the incidence and severity of complications. Finally, a sleep assessment was done by asking the patients to provide the required information. And there was no formal tool used for pain assessment (e.g., Visual Analog Scale) which is crucial for DNP and insomnia relation. However, it would be better to use more objective methods, such as sleepiness and visual analog scales, in further studies.

## CONCLUSION

DPN in older adults may affect the functionality and be associated with fewer sleep hours and depression, independent of DM regulation. In addition to blood glucose regulation, other factors, such as sleep duration and depressed mood, may be associated with DPN in older adults.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was approved by the Clinical Resarches Ethics Committee of the Ankara University Medical Faculty (Date: 13.08.2018, Decision No: 13-878-18).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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