Factors Contributing to Diabetic Peripheral Neuropathy Among Diabetes Mellitus Patients: A Case-Control Study

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Abstract

Background: Diabetes mellitus (DM) is a chronic condition that leads to hyperglycemia due to impaired insulin function. One of the most prevalent and debilitating complications of DM is Diabetic Peripheral Neuropathy (DPN), which significantly contributes to morbidity through sensory, motor, and autonomic nerve dysfunction. In Indonesia, the prevalence of DPN is notably high, with a rising burden of diabetes-related complications. This study aimed to investigate the relationship between various risk factors and the incidence of DPN in a sample of DM patients from Dr. Moewardi Regional Hospital. Methods: A quantitative, observational case-control study was conducted with 64 DM patients, divided into two groups: 32 with DPN and 32 without DPN. Participants were assessed based on education level, smoking status, disease duration, and self-management compliance. Neuropathy was diagnosed using clinical examinations, including sensory (vibration sensation), motor (foot deformities), and autonomic (skin dryness) assessments. Statistical analyses, including chi-square tests and odds ratio calculations, were employed to examine the association between risk factors and DPN. Results: The study found that self-management compliance was strongly associated with DPN (p=0.001), with non-compliant patients having a 3.67 times higher likelihood of developing DPN. Education level showed a non-significant association (p=0.098), though those with lower education levels had a higher risk of DPN (OR=3.22). Duration of DM and smoking status were not significantly related to DPN (p=0.31 and p=1.000, respectively). Conclusion: Effective self-management is a critical factor in preventing DPN in DM patients, as non-compliant individuals are at significantly higher risk. While education level may influence DPN risk, it is not a primary determinant. Early screening, improved awareness, and better self-management education are essential for reducing the incidence of DPN and associated complications in DM patients, particularly in resource-limited settings like Indonesia.

Keywords: Diabetes Mellitus, Diabetic Peripheral Neuropathy, Risk Factors, Self-Management, Education Level

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by persistent hyperglycemia due to impaired insulin secretion, insulin action, or both (ADA, 2021). Recognized as a silent killer, DM often goes undiagnosed until significant complications arise, making it a serious global health challenge (Kemenkes, 2020). Its impact is escalating, particularly in middle- and low-income countries where healthcare resources are often limited (W.H.O.,

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Significance | This study demonstrates the influence of self-management, education, and disease duration on diabetic peripheral neuropathy risk, aiding prevention strategies.

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2019). In 2019, approximately 463 million individuals were living with DM globally, a number projected to rise to 578 million by 2030 and 700 million by 2045 (I.D.F., 2019). Indonesia ranks seventh globally in diabetes prevalence, with 10.7 million affected individuals in 2019, a sharp increase from 6.9% prevalence in 2013 to 8.5% in 2018, according to Riskesdas data (Kemenkes, 2020).

Poorly managed DM leads to acute complications such as hypoglycemia, diabetic ketoacidosis, and hyperosmolar hyperglycemic states, as well as chronic complications, including macrovascular (e.g., coronary artery disease, stroke) and microvascular (e.g., neuropathy, nephropathy, retinopathy) conditions (Cahyono & Purwanti, 2019). Diabetic Peripheral Neuropathy (DPN) is the most prevalent chronic complication of DM, contributing significantly to morbidity through sensory, motor, and autonomic nerve dysfunction (Saranya et al., 2019). Sensory impairment in DPN can result in progressive numbness, often culminating in diabetic foot ulcers (I.D.F., 2019).

The global burden of DPN is substantial. Prevalence estimates indicate that 46% of individuals with diabetes in Africa experience DPN, with the highest rates observed in West Africa (Shiferaw et al., 2020). In Southeast Asia, countries like Malaysia, the Philippines, and Indonesia report the highest prevalence at 54.3%, 58.0%, and 58.0%, respectively (Malik et al., 2020). In Indonesia, neuropathy accounts for 54% of DM-related complications at RSUP Dr. Cipto Mangunkusumo, and 16.2% of DM patients develop diabetic foot ulcers, often necessitating amputation due to inadequate awareness and management of complications (Adi Pamungkas et al., 2022).

Once DPN advances to severe stages, such as ulcers and Charcot foot, the condition becomes challenging to treat, significantly increasing the risk of amputation and mortality (Gylfadottir et al., 2019). Fluctuating blood glucose levels exacerbate neuropathy, leading to more severe outcomes. A study by Liu et al. (2019) identified critical risk factors for DPN, including the duration of diabetes, advanced age, and poor glycemic control, as measured by HbA1c levels. These findings are echoed by other research highlighting that the severity of DPN is influenced by age, Body Mass Index (BMI), and diabetes duration (Amour et al., 2019).

The incidence of DPN underscores the urgent need for proactive measures to mitigate its impact. Screening for risk factors such as glycosylated hemoglobin A1c (HbA1c) levels, diabetic retinopathy, smoking, and BMI is crucial for early detection and prevention of complications (Liu et al., 2019). Preventive interventions aimed at improving glycemic control and managing risk factors can reduce the likelihood of severe outcomes such as diabetic ulcers and amputations.

In Indonesia, the high prevalence of DPN-related complications reflects a lack of comprehensive diabetes education and regular screening programs. Addressing this gap requires coordinated efforts to raise awareness, enhance early detection, and improve access to treatment. Physical examinations and patient history assessments play a pivotal role in identifying individuals at risk of developing DPN. Early intervention strategies targeting modifiable risk factors, including lifestyle modifications and glycemic control, are essential to curb the growing burden of DPN and associated complications.

By focusing on the identification and management of DPN risk factors, healthcare systems can alleviate the social and economic burdens of DM-related complications. Screening and preventive strategies not only improve patient outcomes but also reduce the strain on healthcare resources in low- and middle-income settings. Research and policy initiatives that prioritize early diagnosis and effective management of DPN can significantly enhance the quality of life for individuals with diabetes and mitigate the global burden of this chronic condition.

2. Materials and Methods

2.1 Study Design

This study employed a quantitative research approach with observational analytics, utilizing a case-control research design. Ethical approval for this study was obtained from the Ethics Committee of Dr. Moewardi Regional Hospital. Written informed consent was obtained from all participants prior to their inclusion in the study.

2.2 Population and Sample

The population for this study consisted of diabetes mellitus (DM) patients receiving treatment at Dr. Moewardi Regional Hospital. A total of 64 patients were selected as the study sample, evenly divided into two groups: 32 patients with diabetic motor neuropathy and 32 patients without diabetic motor neuropathy. The inclusion criteria required participants to have a confirmed diagnosis of diabetes mellitus and to either present with or without peripheral neuropathy, as determined through clinical examination. Patients with neurological disorders unrelated to DM and those who declined to participate were excluded from the study.

2.3 Data Collection

Data collection for this study took place from [insert start date] to [insert end date]. Information on risk factors was gathered through questionnaires, which included details about participants' education levels, smoking status, duration of diabetes mellitus (DM), and self-management compliance. Neuropathy assessments were conducted to classify the type and presence of diabetic peripheral neuropathy (DPN). Sensory neuropathy was evaluated using a 128 Hz tuning fork to detect the loss of vibration sensation. Motor neuropathy was assessed by observing foot deformities such as claw toes or hallux valgus. Autonomic neuropathy was determined by examining the skin on the feet for dryness or cracks. Patients were categorized into three types of neuropathy based on

their symptoms: sensory neuropathy indicated by vibration sensation loss, motor neuropathy characterized by visible foot deformities, and autonomic neuropathy evidenced by dry or cracked skin on the feet.

2.4 Statistical Analysis

Data analysis was carried out using SPSS software (version 15). A univariate analysis was conducted to describe the characteristics of the respondents, including their education level, duration of diabetes mellitus (DM), smoking status, and self-management compliance, using descriptive statistics such as frequencies and percentages. Bivariate analysis was performed using chi-square tests to assess the relationships between risk factors and diabetic peripheral neuropathy (DPN), with the significance level set at $\alpha = 0.05$. Additionally, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to identify potential risk factors associated with DPN.

2.5 Ethical Considerations

This study obtained Ethical approval from the Health Research Ethics Committee at Dr. Moewardi General Hospital, Central Java, Indonesia (1.094/XII/HREC/2022). Confidentiality and anonymity of participant data were ensured throughout the study. All procedures adhered to the ethical principles outlined in the Declaration of Helsinki. Participants were informed about the study's purpose, procedures, risks, and benefits. They were free to withdraw at any stage without any repercussions.

3. Results and Discussion

The characteristics of the 64 respondents in this study included education level, duration of diabetes mellitus (DM), smoking status, self-management compliance, and the presence of diabetic peripheral neuropathy (DPN), as summarized in Table 1.

3.1 Relationship Of Factors With The Incidence Of DPN

Relationship of Factors with the Incidence of DPN

A chi-square test with a significance level of $\alpha = 0.05$ was conducted to evaluate the relationship between these factors and the incidence of DPN. The factors analyzed included education level, duration of DM, smoking status, and self-management compliance, with the results presented in Table 2.

Respondents with higher education (minimum undergraduate degree) included 8 individuals without DPN and 3 with DPN. In contrast, among respondents with lower education levels, 24 did not have DPN, while 29 experienced DPN. The chi-square test yielded a p-value of 0.098, indicating no significant relationship between education level and DPN. However, the odds ratio (OR) was 3.22 (95% CI: 0.77–13.50), suggesting that respondents with lower education levels had a 3.22 times higher likelihood of developing DPN compared to those with higher education levels, identifying education level as a potential risk factor.

The duration of DM was categorized into two groups: ≤5 years and >5 years. Among respondents with DM for ≤5 years, 20 did not have DPN, while 16 experienced DPN. For those with DM lasting >5 years, 12 were without DPN, while 16 had DPN. The analysis produced a p-value of 0.31, showing no significant association between the duration of illness and DPN. The OR was 1.67 (95% CI: 0.61–4.51), indicating that respondents with DM for >5 years had a 1.67 times higher risk of developing DPN compared to those with a shorter illness duration.

Among respondents with a smoking habit, 23 did not have DPN, while 23 experienced DPN. Similarly, among non-smokers, 9 did not have DPN, and 9 experienced DPN. The chi-square test resulted in a p-value of 1.000, indicating no significant relationship between smoking status and DPN. The OR was 1.000 (95% CI: 0.336–2.074), suggesting that smoking status did not influence the incidence of DPN.

Self-management compliance showed a notable relationship with DPN. Among non-compliant respondents, 12 did not have DPN, while 32 experienced DPN. In contrast, all 20 compliant respondents were without DPN, and none developed the condition. The chi-square test yielded a p-value of 0.001, demonstrating a significant association between self-management compliance and DPN. The OR was 3.667 (95% CI: 2.262–5.954), indicating that non-compliant individuals had a 3.67 times higher likelihood of developing DPN compared to compliant individuals.

These findings highlight the varying impacts of education level, duration of illness, smoking status, and self-management compliance on the risk of developing DPN, with self-management compliance emerging as the most significant factor.

3.2 Education Level

Education plays a crucial role in shaping an individual's attitudes, behaviors, and ability to process information. A higher education level enables individuals to access and understand knowledge more effectively, while lower education levels may limit the adoption of new values and hinder the understanding of health-related information. Research highlights a significant relationship between education and the management of diabetic neuropathy (Purwanti & Novitasari, 2021). In the current study, education level emerged as a potential risk factor for diabetic peripheral neuropathy (DPN). Respondents with lower education levels were 3.222 times more likely to develop DPN compared to those with higher education, as indicated by an odds ratio (OR) > 1.

Faridi et al. (2020) found that respondents with higher levels of knowledge often did not develop neuropathy, with 84.6% of knowledgeable participants being neuropathy-free. Their chi-square test yielded a p-value < 0.05, indicating a significant relationship between education and neuropathy, though the OR of 0.182 suggests that lower education levels are not necessarily the primary contributors. This discrepancy may arise because diabetes

mellitus (DM) patients often misinterpret neuropathy symptoms, attributing them to other conditions, delaying medical consultation and treatment.

The present analysis further underscores this complexity. While the OR of 3.222 suggests that lower education could contribute to a higher likelihood of DPN, the p-value of 0.098 indicates no statistically significant relationship between education level and DPN. Mizokami-Stout et al. (2020) reinforced this finding, identifying low education as an additional—not primary—risk factor for DPN. Higher education levels in DM patients may enhance their awareness and curiosity about complications, leading them to seek information about DM management (Barbosa et al., 2019). However, such awareness does not always translate into effective self-management.

Wiboworini et al. (2021) observed that even patients with higher education levels may not consistently demonstrate adequate self-management skills necessary for controlling blood sugar. This disconnect suggests that education, while important, does not singularly determine effective DM management or the prevention of DPN. Other factors, including self-management compliance, health system support, and timely access to medical care, play critical roles in mitigating DPN risk.

Overall, while education level contributes to DPN risk, it should not be viewed in isolation, as other factors significantly influence the management and progression of diabetic complications.

3.3 Length of Illness

Diabetic Peripheral Neuropathy (DPN) is a prevalent and debilitating complication of diabetes mellitus (DM) that significantly reduces the quality of life. Monofilament testing has indicated a DPN prevalence of 28.5%, while the EURODIAB IDDM Complications Study reported a 28% prevalence among type 1 DM patients (Elbarsha et al., 2019). The relationship between disease duration and DPN, as assessed through the Diabetic Neuropathy Symptoms (DNS) and Diabetic Neuropathy Examination (DNE) tools, was found to be statistically significant ($\rho < 0.05$). Additionally, increased blood glucose levels are closely linked to aging, contributing to the rising prevalence of diabetes and glucose intolerance with age. Research by Barbosa et al. emphasized that disease duration is strongly associated with the occurrence of DPN (Barbosa et al., 2019). Similarly, Liu et al. highlighted that disease duration significantly influences the development of peripheral neuropathy in type 2 diabetes (Liu et al., 2019).

Globally, the prevalence and incidence of DPN vary widely, ranging from 18.5% to 100%, depending on the duration of DM. Observations from the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) study revealed that at least 20% of type 1 DM patients with a disease duration exceeding 20 years developed DPN. In this study, the disease duration was categorized as either less than

5 years or more than 5 years. The results yielded a p-value of 0.313, indicating no statistically significant relationship between duration of illness and DPN. This may be attributable to late DM diagnoses, whereby patients already experience neuropathy symptoms before their condition is recognized. This late awareness of the disease highlights a societal neglect of DM's impact, often leading to worsening conditions with severe consequences (Miranda & R, 2020).

Early prevention and timely diagnosis of neuropathy are crucial for minimizing its progression and preventing complications such as diabetic ulcers. Delayed diagnosis can exacerbate neuropathy severity, increasing patient morbidity (Purwanti et al., 2024). Although no statistical significance was found in this study, disease duration was identified as a risk factor. An odds ratio (OR) >1 suggests that individuals with a DM duration of more than 5 years are 1.667 times more likely to develop DPN compared to those with a shorter duration. This aligns with findings by Taheri et al., who reported that longer DM duration correlates with a significantly higher risk of DPN ($\rho < 0.001$) (Taheri et al., 2020).

3.4 Smoking Habits

Public awareness of health issues remains inadequate, with many individuals maintaining unhealthy habits and lifestyles such as smoking. One of the diseases that can result from such behaviors is diabetes mellitus (DM), which can lead to complications like Diabetic Peripheral Neuropathy (DPN). The primary risk factors for DPN in DM include age, body mass index (BMI), hypertension, smoking, and waist circumference. Research by Garoushi et al. (2019) highlighted smoking as a significant risk factor for the development of DPN, noting that long-term smoking increases the likelihood of insulin resistance and poor metabolic control. Nicotine, a key component of cigarettes, enters the bloodstream and influences dopamine levels, leading to addiction, reduced appetite, and consequently, poor nutritional habits, all of which can disrupt metabolism (Yesisca & Nataprawira, 2021). The effects of tobacco use may directly involve one or more of its chemical compounds or indirectly exacerbate diabetic neuropathy (Fouchard et al., 2023).

In a recent study, the relationship between smoking and DPN was analyzed, but the results indicated no statistical significance, with a p-value of 1.000. The odds ratio (OR) was found to be 1.000, suggesting that 50% of smoking respondents had an equal chance of developing DPN as non-smokers. However, this lack of significance may be due to the inclusion of case-control studies with limited risk factors and the need for more precise data, such as the duration of smoking. Further research is necessary to explore the connection between smoking and DPN more accurately. Higher-quality analytical or experimental studies with more robust data, including smoking duration on a numerical scale, are required to draw firmer conclusions (Liu et al., 2019).

3.5 Self Management

Table 1. Characteristics of Respondents

Characteristics	Amount	Percentage
Level of education		
No school	6	9.4
Elementary School	16	25
Junior High School	14	21.9
Senior High School	16	25
College/undergraduate	12	18.8
Long Sick		
0-5 years	36	56.3
More than 5 years	28	43.7
Smoking Status		
Not	46	71.9
Yes	18	28.1
Self-Management Compliance		
Not obey	44	68.8
Obey	20	31.2
DPN		
Not experiencing DPN	32	50
Experiencing DPN	32	50

Table 2. Relationship of Risk Factors with the Incidence of DPN

Faktor risiko	DPN		p-value	Odds Ratio (OR)	CI	
	No Incidence DPN	**Incidence DPN**			**Lower**	**Upper**
Level of Education			0,098	3.222	0.769	13.504
High	8	3				
Low	24	29				
Length of Illness			0.313	1.667	0.615	4.513
Less of 5 years	20	16				
More 5 years	12	16				
Smoking Status						
No smoking	23	23	1.000	1.000	0.336	2.074
Smoking	9	9				
Self-management Complience			0.001	3.667	2.262	5.954
No obey	12	32				
Obey	20	0				

Neuropathy is one of the most common microvascular complications of diabetes mellitus (DM), affecting the peripheral, central, and/or autonomic nervous systems. Peripheral neuropathy, in particular, remains one of the most challenging and significant complications for individuals with diabetes, often manifesting in the early stages of dysglycemia, including in the prediabetes phase. It is critical for patients to engage in self-management strategies to regulate their perceptions, behavior, and psychological well-being to effectively manage their chronic diseases, including DM. Self-management refers to the use of scientific and rational methods by patients to take control of their health, which includes behavior modification and lifestyle adjustments to improve health outcomes (Allegrante et al., 2019; Saputra & Rosyid, 2024).

Jaiswal et al. (2020) demonstrated that poor glycemic control is a modifiable risk factor for the development of diabetic peripheral neuropathy (DPN) in both type 1 and type 2 diabetes. Poor glycemic control, as indicated by higher HbA1c levels, is more commonly found in diabetic patients with DPN compared to those without it. Several large-scale studies, such as the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS), have shown that maintaining good glycemic control can significantly delay the onset and progression of DPN and other microvascular complications in diabetic patients. These findings emphasize the importance of diabetes self-management in improving health outcomes, particularly in controlling HbA1c levels. Health literacy and diabetes self-management are closely associated with better glycemic control, with individuals who have higher health literacy being more likely to achieve normal HbA1c levels (Febriani, 2024; Jang et al., 2024).

Several factors can contribute to poor glycemic control, including inadequate patient adherence to prescribed treatment plans, lack of motivation to manage one's health, and limited knowledge about diabetes, its complications, and treatment objectives (Fatimah & Purwanti, 2024). Poor adherence to treatment regimens and lack of knowledge often hinder patients from effectively managing their condition, ultimately contributing to the progression of complications such as DPN. This highlights the importance of early screening and identification of neuropathy in diabetic patients, which provides an opportunity for better glycemic control before significant morbidity arises. Early and accurate diagnosis allows healthcare providers to implement the most appropriate treatment and preventive strategies tailored to the individual patient, thus reducing the potential for severe complications such as diabetic ulcers (Drechsel et al., 2021).

In the present study, statistical analysis revealed a significant relationship between self-management compliance and the occurrence of DPN, with a p-value of 0.001. This suggests that effective self-management is strongly associated with improved glycemic control and a reduced likelihood of developing DPN.

Diabetes self-management encompasses several critical aspects, including adherence to medication regimens, consistent monitoring of diet and blood glucose levels, participation in physical activity, and proper foot care. The compliance factor in self-management serves as a significant risk factor, as indicated by an odds ratio (OR) greater than 1. The OR value of 3.667, with a confidence interval of 2.262-5.954, suggests that non-compliant individuals have 3.667 times the likelihood of developing DPN compared to those who adhere to self-management practices.

Numerous studies have underscored the importance of improving diabetes self-management to achieve better health outcomes and reduce the incidence of complications like DPN (Hurst et al., 2020). Effective diabetes self-management is particularly important for long-term treatment success in DPN patients, as it can delay disease progression and enhance the Health-Related Quality of Life (HRQOL) (Ahmadzadeh et al., 2021; Yuniartika et al., 2023). Ensuring patients understand the value of self-care and adherence to treatment protocols is essential for improving long-term health outcomes.

The present study adopted a quantitative research design, utilizing observational analytics with a case-control design. This allowed for the numerical distribution of variables (in terms of frequency and percentage) and the application of statistical tests to examine the relationships between these variables. The study focused on patients diagnosed with diabetes mellitus at Dr. Regional Hospital, Moewardi, with a total sample size of 64 participants. The case population consisted of 32 individuals with diabetic motor neuropathy, while the control group consisted of 32 individuals without diabetic motor neuropathy. Data collection involved primary data obtained through sensory, motor, and autonomic neuropathy examinations, as well as questionnaires to assess risk factors related to DPN.

The research provides valuable insights into the relationship between education level, self-management compliance, illness duration, and smoking status with the development of DPN in diabetes patients. However, the study's limitations include a small sample size, which may not fully capture the complexity of risk factors influencing DPN. Additionally, the research struggled to adequately assess the impact of smoking duration, as the data did not categorize smoking duration on a numerical scale. It is recommended that future studies increase the sample size to enhance the analysis of risk factors associated with DPN. Furthermore, researchers should consider including a more precise categorization of smoking duration to better understand its relationship with DPN development.

4. Conclusion

In conclusion, this study highlights the critical role of diabetes self-management in reducing the incidence of DPN and improving

health outcomes for patients with diabetes. Improved adherence to treatment protocols, greater health literacy, and consistent monitoring of blood glucose levels are essential for achieving glycemic control and preventing complications. Further research is necessary to explore additional risk factors and refine strategies for managing DPN in diabetic patients, particularly through improved patient education and early diagnosis.

Effective self-management, including glycemic control and lifestyle modifications, plays a crucial role in reducing the risk of Diabetic Peripheral Neuropathy (DPN) in diabetes patients. This study identified non-compliance with self-management as a significant factor in the development of DPN, emphasizing the importance of patient education and regular health monitoring. While education level and disease duration also influence DPN risk, self-management emerged as the most impactful factor. These findings underline the need for comprehensive diabetes education and preventive strategies to mitigate the global burden of DPN.

Author contributions

O.S.P. conceptualized the study and supervised the research process. A.S. contributed to the methodology and data curation. B.K. and V.Y. were responsible for the investigation and formal analysis. A.M. assisted in data validation and project administration. M.F. contributed to software and visualization. E.Y. drafted the manuscript and coordinated the writing process. All authors reviewed and approved the final manuscript.

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Competing financial interests

The authors have no conflict of interest.

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