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FACTORS ASSOCIATED DIABETIC NEUROPATHY AND PERIPHERAL ARTERY DISEASE IN PATIENTS TYPE 2 DIABETES MELLITUS AT DIABETIC CENTER CLINIC NGOERAH HOSPITAL DENPASAR

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ABSTRACT

Background: Diabetes mellitus (DM) is a leading cause of mortality worldwide. Diabetic foot is a common complication of DM, as it mainly connects to diabetic neuropathy (DN) and peripheral arterial disease (PAD). **Objective:** This study aimed to evaluate the interaction between multiple causes of DN and PAD of T2DM patients in Ngoerah Hospital, Denpasar. **Methods:** A cross-sectional study was conducted during August–October 2024 on 200 T2DM patients (30–70 years of age). Risk factors evaluated included but were not limited to gender, age, smoking, glycemic control, duration of DM, hypertension, obesity and dyslipidemia. DN was measured by DNS-Ina and DNE-Ina, whereas PAD was assessed with ankle-brachial index (ABI). Bivariate analysis was performed using chi-square and independent t-tests and multivariate logistic regression statistics in SPSS version 27.0. **Results:** There was a significant association of DN in 117 patients (58.5%) and PAD in 118 patients (59%). Gender, DM duration and obesity were associated with DN ($p = 0.019$, $p = 0.013$, $p = 0.013$) and PAD ($p = 0.002$, $p = 0.037$, $p = 0.042$), respectively. Multivariate analyses revealed that gender, DM duration, and obesity were independently associated with DN ($p = 0.034$, $p = 0.027$, $p = 0.027$), whereas PAD was significantly associated only with gender ($p = 0.003$). **Conclusions:** Independent factors of gender, duration of diabetes, and obesity predict diabetic neuropathy, with significant gender differences in predicting PAD in T2DM.

Keywords:

*Diabetes Mellitus,
Diabetic Neuropathy,
Peripheral Arterial Disease.*

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INTRODUCTION

Diabetes mellitus (DM) is one of the top 10 leading causes of death, with more than 6.7 million people aged 20–79 years dying from DM-related complications. The International Diabetes Federation (IDF) reported that the global prevalence of DM reached 537 million people in 2021 and is projected to rise to 643 million by 2030 and 783 million (a 46% increase) by 2045. In Indonesia, the prevalence of DM has increased to 19.5 million people, compared to 10.7 million in 2019. Indonesia ranks fifth in the world for the highest number of DM cases,

previously ranking seventh¹. The 2023 Indonesian Health Status (Status Kesehatan Indonesia, SKI) reported an increase in diabetes prevalence based on physician diagnosis, rising from 2% in 2018 to 2.2% in 2023 among individuals aged ≥ 15 years. In Bali Province, the prevalence increased from 1.3% in 2018 to 1.7% in 2023 in the same age group².

Diabetic foot is a complication of DM that affects the lower extremities, characterized by microangiopathy (neuropathy) and macroangiopathy (peripheral artery disease), leading to increased morbidity, mortality, and economic burden in the



future. The global prevalence of diabetic foot is estimated to be 40–60 million cases³. In Indonesia, the prevalence of diabetic foot classified as Wagner stage III or higher at Wahidin Sudirohusodo Hospital, South Sulawesi, exceeds 68%, with 55% of cases requiring debridement and amputation⁴. At Buleleng General Hospital, Bali, diabetic foot cases classified as Wagner stage III and IV accounted for 40.7% and 32.2%, respectively, with 74.3% of cases undergoing amputation⁵.

Diabetic neuropathy (DN) is a microangiopathic complication of DM that is not associated with other causes of neuropathy. Distal sensorimotor polyneuropathy (DSPN) affects one-third of DM patients, with an incidence rate of approximately 2% per year⁶. According to data from the International Diabetes Federation (2021), the prevalence of diabetic neuropathy in Indonesia is approximately 17.6%. Hospital records from Ngoerah Hospital indicate that 7.6% of DM patients experience DN.

Peripheral artery disease (PAD) is one of the three clinical manifestations of arteriosclerosis, significantly reducing quality of life and limiting physical activity. The global prevalence of PAD exceeds 230 million cases. A study reported that patients with uncontrolled DM have a 10-fold increased risk of developing PAD compared to non-DM patients⁷. Another study found that the prevalence of PAD in Southeast Asia between 1990 and 2019 was approximately 4.2%, with an incidence rate of 2.1% and a mortality rate of 52.9% per 100,000 people⁸. Additionally, a study conducted at the Diabetes Clinic of Ngoerah Hospital, Denpasar, reported a PAD prevalence of 45.8% during the period of June–August 2016⁹.

These data indicate that type 2 DM and its complications remain inadequately controlled, with rising incidence over time. There have been other works that have suggested diabetic neuropathy and peripheral arterial disease risk factors, but the available risk factors are mostly obtained in Western populations, which may not fully capture the clinical features of Indonesian patients. Furthermore, limited local data are available using standardized diagnostic tools such as DNS-Ina, DNE-Ina, and ABI in routine clinical settings. Consequently, this study will examine the characteristics and factors associated with DN and PAD among patients with type 2 DM at

Ngoerah Hospital, Denpasar, in order to offer context-specific evidence for early detection and prevention.

METHODS

This study was designed as an analytical observational study employing a cross-sectional approach to investigate the relationships between various risk factors and the occurrence of diabetic neuropathy (DN) and peripheral artery disease (PAD) in patients with type 2 diabetes mellitus (T2DM). The research was conducted at the Diabetes Center Clinic of Ngoerah Hospital, Denpasar, Indonesia, which serves as a referral center for diabetes management in the region.

The target population in this study comprised all patients diagnosed with type 2 diabetes mellitus (T2DM) who visited the Diabetes Center Clinic of Ngoerah Hospital between August and October 2024. The study sample consisted of patients who met the predetermined inclusion criteria, which included individuals aged 30 to 70 years, those who were cooperative, willing to participate, and who provided signed informed consent. Meanwhile, patients who met the exclusion criteria were not included in the study. The exclusion criteria encompassed patients presenting with acute infections, pregnancy, a history of foot amputation or previous surgical procedures, individuals with a history of alcohol consumption, stroke, malignancy, HIV infection, or those who had undergone neurotoxic drug treatment. These criteria were applied to ensure the reliability of the study findings and to minimize potential confounding factors.

In this study, the dependent variables consisted of diabetic neuropathy (DN) and peripheral artery disease (PAD), which were assessed based on established clinical criteria. The independent variables examined included age, gender, smoking habits, duration of diabetes mellitus, glycemic control, hypertension, dyslipidemia, and obesity, as these factors have been widely recognized as potential contributors to the development of DN and PAD. Additionally, control variables were considered to account for potential confounding factors, which included acute infections, pregnancy, prior history of amputation or surgical interventions, alcohol consumption, stroke, malignancy, HIV infection, and neurotoxic drug treatments.



Data collection was conducted through a combination of questionnaires and secondary data extraction from electronic medical records (SIMARS system) at Ngoerah Hospital, Denpasar. The collected data encompassed sociodemographic variables, including age, gender, and smoking habits, as well as clinical parameters such as glycemic control (measured by DM duration) and the presence of comorbid conditions (including hypertension and dyslipidemia). Additional laboratory data, such as HbA1c levels and lipid profiles, were retrieved from medical records within the last three months, ensuring the accuracy of metabolic status assessment. Anthropometric measurements, including height and weight, were performed using standardized equipment such as a Seca scale and Microtoise, which were available at the Diabetes Center Clinic.

Diabetic neuropathy (DN) was evaluated using the DNE-Ina questionnaire, along with a thorough neurological examination conducted at the Diabetes Center Clinic. The peripheral artery disease (PAD) diagnosis was established through the ankle-brachial index (ABI) measurement using an ultrasound Doppler ABI device. The neurological examination for DN included a reflex hammer test, pinprick sensation assessment, 128 Hz tuning fork vibration test, and the Semmes-Weinstein 10-g monofilament test to assess sensory impairment. All assessments were conducted by trained medical personnel and followed standardized diagnostic procedures to ensure the validity and reproducibility of the findings.

The statistical analysis was conducted in several steps to provide a comprehensive interpretation of the data. Descriptive statistics were utilized to present the baseline characteristics of the study population, allowing for a clear understanding of the distribution of various risk factors. Bivariate analysis was performed using Chi-Square and Fisher's Exact tests, with statistical significance defined as $p < 0.05$. To further explore the independent associations between risk factors and DN/PAD, multivariate analysis was conducted using a logistic regression model, where a significance level of $p < 0.05$ was maintained. All statistical computations were carried out using SPSS software version 27.0.

RESULTS

This study analyzed 200 patients diagnosed with type 2 diabetes mellitus (T2DM) who visited the Diabetes Center Clinic at Ngoerah Hospital, Denpasar, between August and October 2024. The distribution of diabetic neuropathy (DN) and peripheral artery disease (PAD), as well as the demographic and clinical characteristics of the study population, were assessed. Among the total subjects, 117 patients (58.5%) were diagnosed with DN, while 83 patients (41.5%) did not present with DN. Similarly, 118 patients (59%) were found to have PAD, whereas 82 patients (41%) did not have PAD.

In terms of age distribution, 51 patients (25.5%) were aged between 30 and 50 years, while the majority, 149 patients (74.5%), were between 51 and 70 years old. Regarding gender, 82 patients (41%) were female, whereas 118 patients (59%) were male. Smoking habits were also assessed, revealing that 99 patients (49.5%) were smokers, while 101 patients (50.5%) were non-smokers. The duration of diabetes was categorized into two groups, with 132 patients (66%) having had diabetes for less than 10 years and 68 patients (34%) living with diabetes for 10 years or more.

Glycemic control was evaluated using HbA1c levels, showing that 35 patients (17.5%) had good glycemic control, whereas 165 patients (82.5%) had poor glycemic control. Hypertension was present in 118 patients (59%), while 82 patients (41%) had no history of hypertension. Dyslipidemia was highly prevalent in this study population, with 191 patients (95.5%) diagnosed with dyslipidemia, whereas only 9 patients (4.5%) had normal lipid profiles. Obesity was another key factor observed, with 83 patients (41.5%) classified as obese and 117 patients (58.5%) having a normal or underweight body mass index (BMI).



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Table 1. Characteristics of Subjects

Variable	Total (n=200)	DN		PAP	
		Yes, n (%) 117 (58,5%)	No, n (%) 83 (41,5%)	Yes, n (%) 118 (59%)	No, n (%) 82 (41%)
Age (years), median (min-max)	57 (30-70)	58 (35-70)	56 (30-70)	58 (32-70)	56 (30-70)
51-70, n (%)	149 (74,5%)	85 (72,9%)	64 (77,1%)	88 (74,6%)	61 (74,4%)
30-50, n (%)	51 (25,5%)	32 (27,4%)	19 (22,9%)	30 (25,4%)	21 (25,6%)
Gender					
Female, n (%)	82 (41%)	56 (47,9%)	26 (31,3%)	59 (50%)	23 (28%)
Male, n (%)	118 (59%)	61 (52,1%)	57 (68,7%)	59 (50%)	59 (72%)
Smoking Habit					
Smoker, n (%)	99 (49,5%)	60 (51,3%)	39 (47%)	57 (48,3%)	42 (51,29%)
Non Smoker, n (%)	101 (50,5%)	57 (48,7%)	44 (53%)	61 (51,7%)	40 (48,8%)
Duration of DM (Month), median (min-max)	60 (1-480)	60 (1-480)	60 (1-480)	66 (1-480)	48 (1-480)
≥10 years, n (%)	68 (34%)	48 (41%)	20 (24,1%)	47 (39,8%)	21 (25,6%)
<10 years, n (%)	132 (66%)	69 (59%)	63 (75,9%)	71 (60,2%)	61 (74,4%)
HbA1c (%), median (min-max)	8,6 (5-14)	8,9 (5-14)	8,4 (5,6-14)	8,7 (5-14)	8,55 (5-14)
Glicemic Control					
Poor, n (%)	165 (82,5%)	100 (85,5%)	65 (78,3%)	101 (85,6%)	64 (78,8%)
Good, n (%)	35 (17,5%)	17 (14,5%)	18 (21,7%)	17 (14,4%)	18 (22%)
Systolic Blood Pressure (mmHg), median (min-max)	120 (90-180)	120 (90-180)	124 (90-180)	120 (90-180)	122 (90-170)
Diastolic Blood Pressure (mmHg), median (min-max)	77,5 (52-114)	76 (52-109)	78 (56-114)	77,5 (52-100)	77,5 (56-114)
Hypertension					
Yes, n (%)	118 (59%)	67 (57,3%)	51 (61,4%)	66 (55,9%)	52 (63,4%)
No, n (%)	82 (41%)	50 (42,7%)	32 (38,6%)	52 (44,1%)	30 (36,6%)
Total Cholesterol (mg/dL), median (min-max)	171 (61-366)	162 (61-366)	180 (86-310)	162,5 (61-366)	178 (76-291)
LDL Cholesterol (mg/dL), median (min-max)	99,5 (12-313)	98 (12-313)	101 (31-242)	99,5 (12-313)	99,5 (31-242)
HDL Cholesterol (mg/dL), median (min-max)	34 (6-76)	32 (6-76)	36 (8-58)	32,5 (6-76)	34,5 (8-58)
Triglycerides (mg/dL), median (min-max)	127,7 (33-545)	136 (33-479)	125 (45-545)	132,5 (33-479)	124 (45-545)



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Dyslipidemia					
Yes, n (%)	191 (95,5%)	111 (94,9%)	80 (96,4%)	111 (94,1%)	80 (97,6%)
No, n (%)	9 (4,5%)	6 (5,1%)	3 (3,6%)	7 (5,9%)	2 (2,4%)
Body Mass Index (kg/m ²), median (min-max)	23,9 (16,2-37,5)	23,9 (16,2-36,5)	25(17,9-37,5)	23,9 (16,20-36,5)	24,9 (17,6-37,5)
Obesity					
Yes, n (%)	83 (41,5%)	40 (34,2%)	43 (51,8%)	42 (35,6%)	41 (50%)
No, n (%)	117 (58,5%)	77 (65,8%)	40 (48,2%)	76 (64,4%)	41 (50%)

DN, Diabetic Neuropathy; PAD, Peripheral Artery Disease; DM, Diabetes Mellitus; HbA1c, Glycated Hemoglobin A1c; LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein.



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Association of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity with Diabetic Neuropathy

A bivariate analysis was conducted to assess the association between age, gender, smoking habits, duration of DM, glycemic control, hypertension, and obesity with the occurrence of DN using the Chi-

square test. Meanwhile, the association between dyslipidemia and DN was analyzed using Fisher's exact test. The table below (Table 2) presents the association between the independent variables (age, gender, smoking habits, duration of DM, glycemic control, hypertension, dyslipidemia, and obesity) and the occurrence of DN.

Table 2. Association of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity with Diabetic Neuropathy

Variabel	Diabetic Neuropathy		PR	95% CI	p
	Yes n=117	No n=83			
Age (years)					
51-70 years	85 (57%)	64 (43%)	0,90	0,706-1,171	0,476 ^a
30-50 years	32 (62,7%)	19 (37,3%)			
Gender					
Female	56 (68,3%)	26 (31,7%)	1,321	1,051-1,660	0,019 ^{*a}
Male	61 (51,7%)	57 (48,3%)			
Smoking Habits					
Smoker	60 (60,6%)	39 (39,4%)	1,074	0,850-1,357	0,550 ^a
Non Smoker	57 (56,4%)	44 (43,6%)			
Duration of DM					
≥10 years	48 (70,6%)	20 (29,4%)	1,350	1,080-1,689	0,013 ^{*a}
<10 years	69 (52,3%)	63 (47,7%)			
Glicemic Control					
Poor	100 (60,6%)	65 (39,4%)	1,248	0,868-1,793	0,189 ^a
Good	17 (48,6%)	18 (51,4%)			
Hypertension					
Yes	67 (56,8%)	51 (43,2%)	0,931	0,737-1,177	0,554 ^a
no	50 (61%)	32 (39%)			
Dyslipidemia					
Yes	111 (58,1%)	80 (41,9%)	0,872	0,541-1,405	0,738 ^b
No	6 (66,7%)	3 (33,3%)			
Obesity					
Yes	40 (48,2%)	43 (51,8%)	0,732	0,565-0,948	0,013 ^{*a}
No	77 (65,8%)	40 (34,2%)			

*Significant; PR, prevalence ratio; ^aChi-Square Test; ^bFisher's Exact Test

Association of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity with Peripheral Artery Diseases

A bivariate analysis was conducted to examine the association between age, gender, smoking habits, duration of DM, glycemic control, hypertension, dyslipidemia, and obesity as risk factors for peripheral artery disease (PAD) in patients with type 2 DM. The bivariate analysis was performed using the Chi-square test and Fisher's exact test. The table below (Table 3) presents the association between the independent variables and the occurrence of PAD.

In this study, subjects in the 51–70 age group who experienced PAD (59.1%) were more prevalent than those without PAD (40.9%), but there was no significant association between age and the occurrence of PAD ($p=0.976$). Male subjects had an equal prevalence of PAD, whereas female subjects with PAD (72%) were more prevalent than those without PAD (28%). A significant association was found between gender and the occurrence of PAD ($p=0.002$). Subjects with a smoking habit had a higher prevalence of PAD (57.6%) compared to those without PAD (42.4%), but there was no significant association between smoking habits and the occurrence of PAD ($p=0.685$). Subjects with a DM duration of ≥ 10 years



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had a higher prevalence of PAD (69.1%) compared to those without PAD (30.9%), and a significant association was found between DM duration and the occurrence of PAD ($p=0.037$).

Subjects with poor glycemic control had a higher prevalence of PAD (61.2%) compared to those without PAD (38.8%), but there was no significant association between glycemic control and the occurrence of PAD ($p=0.167$). Subjects with hypertension who experienced PAD (55.9%) were more prevalent than those without PAD (44.1%), but no significant association was found between

hypertension and the occurrence of PAD ($p=0.290$). Subjects with dyslipidemia who experienced PAD (58.1%) were more prevalent than those without PAD (41.9%), but no significant association was found between dyslipidemia and the occurrence of PAD ($p=0.313$). Subjects with obesity who experienced PAD (50.6%) were more prevalent than those without PAD (49.4%), and a significant association was found between obesity and the occurrence of PAD ($p=0.042$).

Table 3. Association of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity with Peripheral Artery Disease

Variabel	Peripheral Artery Disease		PR	95% CI	p
	Ya n=118	Tidak n=82			
Age (years)					
51-70 years	88 (59,1%)	61 (40,9%)	1,004	0,770-1,310	0,976 ^a
30-50 years	30 (58,8%)	21 (41,2%)			
Gender					
Female	59 (72%)	23 (28%)	1,439	1,149-1,803	0,002 ^{*a}
Male	59 (50%)	59 (50%)			
Smoking Habits					
Smoker	57 (57,6%)	42 (42,4%)	0,953	0,756-1,201	0,685 ^a
Non Smoker	61 (60,4%)	40 (39,6%)			
Duration of DM					
≥10 years	47 (69,1%)	21 (30,9%)	1,285	1,027-1,608	0,037 ^{*a}
<10 years	71 (53,8%)	61 (46,2%)			
Glycemic Control					
Poor	101 (61,2%)	64 (38,8%)	1,260	0,878-1,810	0,167 ^a
Good	17 (48,6%)	18 (51,4%)			
Hypertension					
Yes	66 (55,9%)	52 (44,1%)	0,882	0,701-1,110	0,290 ^a
no	52 (63,4%)	30 (36,6%)			
Dyslipidemia					
Yes	111 (58,1%)	80 (41,9%)	0,747	0,516-1,081	0,313 ^b
No	7 (77,8%)	2 (22,2%)			
Obesity					
Yes	42 (50,6%)	41 (49,4%)	0,779	0,606-1,001	0,042 ^{*a}
No	76 (65%)	41 (35%)			

*Significant; PR, prevalence ratio; ^aChi-Square Test; ^bFisher's Exact Test

Multivariate Analysis of the Effect of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity on Diabetic Neuropathy

A multivariate analysis was conducted to examine the effect of age, gender, smoking habits, duration of DM, glycemic control, hypertension, dyslipidemia, and obesity on diabetic neuropathy

(DN). The multivariate analysis was performed using logistic regression with the backward method. The results indicated that gender, duration of DM, and obesity had a significant positive association with the occurrence of DN ($p = 0.034, 0.027, \text{ and } 0.027$, respectively). The detailed results of the multivariate analysis are presented in Table 4.



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Table 4. Multivariate Analysis of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity on Diabetic Neuropathy

	Diabetic Neuropathy	Coefficient B	OR	95% CI	p
Initial Stage	Gender	0,614	1,848	0,994-3,435	0,052
	Glycemic Control	0,235	1,264	0,576-2,773	0,558
	Duration of DM	0,700	2,013	1,059-3,828	0,033
	Obesity	0,669	1,952	1,081-3,524	0,027
Final Stage	Gender	0,655	1,925	1,051-3,525	0,034*
	Duration of DM	0,720	2,055	1,084-3,895	0,027*
	Obesity	0,667	1,947	1,079-3,514	0,027*

*Significant; OR, *odds ratio*; CI, *confident interval*. References: Female, Obesity, Poor Glycemic Control, Duration of DM \geq 10 years

Multivariate Analysis of the Effect of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity on Peripheral Artery Disease

A multivariate analysis was conducted to assess the association between age, gender, smoking habits, duration of DM, glycemic control, hypertension, dyslipidemia, and obesity with peripheral artery

disease (PAD). The multivariate analysis was performed using logistic regression with the backward method. The results indicated that gender had a significant positive association with the occurrence of PAD ($p = 0.003$). The detailed results of the multivariate analysis are presented in Table 5.

Table 5. Multivariate Analysis of Age, Gender, Smoking Habits, Duration of DM, Glycemic Control, Hypertension, Dyslipidemia, and Obesity on Peripheral Artery Disease

	Peripheral Artery Disease	Coefficient B	OR	95% CI	P
Initial Stage	Gender	0,873	2,393	1,279-4,478	0,006
	Glycemic Control	0,206	1,229	0,562-2,689	0,605
	Duration of DM	0,568	1,766	0,930-3,353	0,082
	Obesity	0,531	1,701	0,940-3,079	0,079
Final Stage	Gender	0,921	2,511	1,368-4,610	0,003*

*Significant; OR, *odds ratio*; CI, *confident interval*. References: Female, Obesity, Poor Glycemic Control, Duration of DM \geq 10 years

DISCUSSION

This study aimed to analyze the factors associated with the occurrence of diabetic neuropathy (DN) and peripheral artery disease (PAD) in patients with type 2 diabetes mellitus (T2DM) at the Diabetes Center Clinic of Ngoerah Hospital, Denpasar. Based on the study findings, gender, DM duration, and obesity were significantly associated with the occurrence of DN and PAD.

Subject Characteristics

This study reveals a strikingly high prevalence of chronic complications among T2DM patients at the Diabetes Center Clinic of Ngoerah Hospital, with Diabetic Neuropathy (DN) affecting 58.5% and Peripheral Artery Disease (PAD) affecting 59% of the study population. These figures are higher than many global averages, which typically cite DN prevalence around 30-50%. The findings in this study align more closely with Simanjuntak and Simamora

(2020), who observed a 54.7% prevalence in North Sumatra.

The study included 200 patients with T2DM aged between 30 and 70 years. The majority of subjects were over 50 years old, with a higher proportion of males than females. Smoking habits were observed in nearly half of the respondents, while most patients had poor glycemic control, hypertension, and dyslipidemia. A study by Simanjuntak and Simamora reported a 54.7% prevalence of DN among T2DM patients at RSU Sari Mutiara Medan, consistent with the findings of this study¹⁰.

This high prevalence at a tertiary referral center like Ngoerah Hospital suggests that many patients arriving at the clinic are already in advanced stages of the disease. The synergy of poor glycemic control (HbA1c $>7\%$), hypertension, and dyslipidemia observed in the majority of subjects creates a "toxic triad" that accelerates both microvascular and macrovascular damage. Additionally, research by



Kuswardhani and Suastika indicated that older age and poor glycemic control significantly increased the risk of PAD¹¹.

Association of Risk Factors with DN and PAD

Bivariate analysis revealed that female patients had a higher risk of DN compared to males. This finding aligns with the study by Gylfadottir et al., which reported a higher prevalence of DN in female T2DM patients compared to males¹². Hormonal factors and differences in body fat distribution may contribute to the increased risk of microvascular complications in females. Similarly, research by Aleidan et al. found that females with T2DM had a higher prevalence of DN, with obesity and poor glycemic control as major risk factors¹³. Ezekia and Dwipayana also reported a higher prevalence of DN in T2DM patients with hypertension compared to those without hypertension⁹.

The significant association between DM duration >10 years and both DN and PAD ($p < 0.05$) underscores the concept of Metabolic Memory. Even if current glycemic control is improved, the legacy effect of prior years of hyperglycemia continues to drive damage.

Furthermore, having T2DM for more than 10 years was significantly associated with an increased risk of DN and PAD, suggesting that the longer a person has DM, the higher the likelihood of vascular and neuropathic complications. Pop-Busui et al. found that the incidence of DN increases significantly in patients with DM duration of more than 10 years, with a prevalence exceeding 50% after 15 years of diagnosis¹⁴. This is also supported by the study by Asir et al., which concluded that T2DM patients with a disease duration of more than 10 years had a higher risk of DN, particularly if they did not achieve optimal glycemic control¹⁵.

Obesity was significantly associated with Diabetic Neuropathy (DN) in this study ($p=0.013$ in bivariate; $p=0.027$ in multivariate), reflecting the contemporary understanding that obesity is not merely a weight-related concern but a state of chronic systemic inflammation that actively drives neurovascular damage. This is primarily mediated through the mechanism of lipotoxicity, where high levels of circulating free fatty acids (FFAs) in obese patients act as metabolic stressors that trigger Toll-

like receptor 4 (TLR4) on Schwann cells and axons, thereby initiating a destructive inflammatory cascade that ultimately leads to the apoptosis of nerve cells. Beyond its neuropathic impact, obesity significantly contributes to the development of Peripheral Artery Disease (PAD) through detrimental structural and biochemical changes, as fat accumulation promotes a pro-thrombotic environment and impairs nitric oxide (NO) bioavailability, which is essential for maintaining proper vasodilation. These findings are highly consistent with the research by Criqui et al. (2021), who emphasized that obesity-driven inflammation serves as a primary driver of atherosclerotic progression in the lower extremities, illustrating how the interplay between metabolic dysfunction and vascular impairment exacerbates the risk of chronic complications in the diabetic population at Ngoerah Hospital.

Multivariate Analysis

One of the most critical findings of this study, as highlighted in the multivariate analysis, is that female gender serves as a significant independent risk factor for both Diabetic Neuropathy (DN) and Peripheral Artery Disease (PAD). This vulnerability is deeply rooted in the hormonal shifts and altered adipose tissue distribution characteristic of post-menopausal women, who constitute the majority of this study's demographic (aged over 50 years). While estrogen typically provides a degree of vascular protection in pre-menopausal individuals, this biological advantage is often abolished in the presence of Type 2 Diabetes Mellitus (T2DM), and the subsequent transition to a post-menopausal state triggers a physiological shift from subcutaneous to visceral fat accumulation. This visceral fat is highly metabolically active and secretes elevated levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha), which directly contribute to chronic systemic inflammation, endothelial dysfunction, and accelerated nerve fiber degradation. This biochemical susceptibility is further complicated by the silent clinical presentation of PAD in women; as noted by Lin et al. (2018), female patients are significantly more likely to remain asymptomatic or present with atypical symptoms rather than the classic claudication often observed in men, who may show more obvious symptoms due to higher physical activity levels or



smoking history. Consequently, women may experience a faster functional decline despite the lack of textbook symptoms, and the multivariate result identifying gender as the sole remaining significant factor for PAD suggests that in the specific population at Ngoerah Hospital, biological sex exerts a more dominant influence on vascular and neuropathic risk than traditional factors such as smoking or hypertension.

The results of logistic regression analysis showed that gender, DM duration, and obesity were independent risk factors associated with DN. Meanwhile, for PAD, only gender remained significant in the multivariate model, suggesting that other factors may have a greater influence on PAD occurrence than the analyzed variables. Lin et al. also found that females were more likely to develop PAD than males, although often asymptomatic⁸. The study by Ezekia and Dwipayana found that the prevalence of PAD at the Diabetes Clinic of Ngoerah Hospital, Denpasar, reached 45.8%, with hypertension and DM duration of more than 10 years as major risk factors⁹. Furthermore, the study by Kuswardhani and Suastika indicated that elderly patients with T2DM who had low triglyceride levels and high homocysteine levels were at a higher risk of developing PAD¹¹.

Study Limitations

This study has several limitations. The cross-sectional design does not allow for determining a causal relationship between risk factors and the occurrence of DN or PAD. Additionally, other factors such as physical activity, dietary patterns, and pharmacological therapy were not thoroughly analyzed in this study. Further research using a longitudinal design may provide better insights into the causal relationship between risk factors and DM complications. The study by Asir et al., which examined the relationship between glycemic control and DN incidence at RSCM, also stated that poor glycemic control was associated with a 30.6% increase in DN risk, reinforcing the findings of this study¹⁵.

CONCLUSION

Gender, DM duration, and obesity were significantly associated with the occurrence of DN in patients with T2DM. For PAD, gender remained the

only significant risk factor in the multivariate analysis. These findings emphasize the importance of early screening and risk factor management to prevent the progression of complications in patients with T2DM.

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ETHICAL APPROVAL

This study was approved by the Research Ethics Commission, approval number 1041/UN14.2.2.VII.14/LT/2024.

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AUTHOR CONTRIBUTIONS

IMPDP: co-author and corresponding author; TIRPP: first author; IPEWD: co-author; WG: co-author; MRS: co-author; IMSS: co-author; IBAN: co-author; KS: co-author. All of the authors collaborated in the study design, execution, and follow-up of the clinical cases, data analysis and results formulation, and writing of the publication. All authors have authorized the submission of the work. The manuscript has neither been published nor submitted elsewhere for publication. The final manuscript was reviewed and approved by all writers.

CONFLICTS OF INTEREST

All authors declare there are no conflict of interest.

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