Prevalence of peripheral arterial disease and peripheral neuropathy in diabetic foot infection in Makassar, Indonesia: A cross-sectional study

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Prevalence of peripheral arterial disease and peripheral neuropathy in diabetic foot infection in Makassar, Indonesia: A cross-sectional study

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ABSTRACT

Background and objectives. Diabetic foot is a debilitating condition that affects approximately 15% of patients with diabetes mellitus (DM) and is frequently complicated by infections. This condition significantly contributes to the high morbidity and mortality rates in DM patients. Numerous studies have identified peripheral arterial disease (PAD) and peripheral neuropathy (PN) as significant risk factors for the development of diabetic foot. Therefore, this study aims to determine the prevalence of PAD and PN in infected diabetic foot.

Materials and methods. This study included 99 patients diagnosed with DM. Participants were categorized into three groups: no diabetic foot, uninfected diabetic foot, and infected diabetic foot. PAD was assessed using the ankle-brachial index measured with a

handheld Doppler device. The presence of PN was evaluated using the Semmes-Weinstein 5.07 (10 g) monofilament.

Results. The prevalence of PAD was significantly higher in patients with infected diabetic foot (84.8%) compared to those with uninfected diabetic foot (66.7%) and those without diabetic foot (15.2%) ($p<0.001$). Similarly, the prevalence of PN was highest among patients with infected diabetic foot (93.9%) ($p<0.001$). The coexistence of PAD and PN was most prevalent in patients with infected diabetic foot, with 78.8% exhibiting both conditions, followed by patients with uninfected diabetic foot (54.5%), and only 6.1% of patients without diabetic foot had both conditions ($p<0.001$).

Conclusions. The prevalence of peripheral arterial disease and peripheral neuropathy were highest in patients with infected diabetic foot, compared to those with uninfected diabetic foot or no diabetic foot.

Keywords: diabetic foot infection, peripheral arterial disease, peripheral neuropathy.

Abbreviations:

DM – diabetes mellitus,

PAD – peripheral arterial disease,

PN – peripheral neuropathy,

DFU – diabetic foot ulcers,

BMI – body mass index,

HbA1c – Hemoglobin A1c,

INTRODUCTION

Diabetic foot ulcers (DFU) are the leading cause of lower extremity amputation in individuals with diabetes mellitus (DM), especially when accompanied by infection (Syauta et al., 2021). It is a major risk factor associated with high rates of disability, mortality, and morbidity among diabetic patients (Khanna et al., 2022; Tuttolomondo et al., 2015). Data indicate that diabetes accounts for 80% of non-traumatic amputation cases, with 85% of these cases involving foot ulcers. Approximately 15% of patients with DM are expected to develop diabetic foot during the disease (Lim et al., 2017; Tuttolomondo et al., 2015).

DFU are a complex, multifactorial condition with interrelated causes that contribute to ulcer development in diabetic patients. Risk factors for DFU include male sex, diabetes duration of more than 10 years, peripheral neuropathy (PN), foot deformities, peripheral arterial disease (PAD), smoking, a history of previous ulcers or amputations, and inadequate glycaemic control (Tresierra-Ayala & García Rojas, 2017). In patients with DM, vasculopathy leading to PAD can significantly increase morbidity and mortality, particularly due to diabetic foot complications. PAD often presents without symptoms because PN reduces touch sensitivity, causing some patients first to notice the condition only when ischemic ulcers or gangrene develop (Pitocco et al., 2019). PN is the most common complication among diabetic patients, progressively affecting the distal regions of the lower extremities. Previous studies indicate that PN and foot infections, often resulting from minor foot trauma, are the leading causes of amputations in diabetic patients (Lawrence et al., 2022; Manoj Abraham et al., 2022; Wukich et al., 2022).

The risk of infection in diabetic foot is multifactorial, influenced by the quantity and virulence of microorganisms present in the ulcer and the host's ability to combat the infection (Hurlow et al., 2018). Elevated blood glucose levels, as seen in DM patients, can substantially impair immune function, increasing susceptibility to ulcer infections (Hurlow et al., 2018; Nursyamsi et al., 2018).

PAD and PN have been identified as significant risk factors for diabetic foot (Liu et al., 2022). These conditions often contribute to the development and progression of infections, posing serious challenges in diabetic foot management. In this study, we aimed to explore the prevalence of these conditions in individuals with infected diabetic foot. Specifically, we assessed the prevalence of PAD, PN, and the coexistence of both conditions in individuals with infected diabetic foot. This comprehensive analysis seeks to provide valuable insights into the interaction of PN and PAD in the context of diabetic foot infections, with the goal of improving prevention and management strategies.

MATERIALS AND METHODS

This cross-sectional study was conducted at Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital in Makassar, Indonesia, involving 99 patients who provided informed consent to participate. The inclusion criteria required participants to be 18 years old or older at the time of examination and to have a confirmed diagnosis of DM, with or without DFU. Patients with a history of limb amputation or the presence of ulcers at the examination sites were excluded from the study. The minimum required sample size, calculated using a standard formula, was 87 participants. A purposive sampling method was used to recruit the study participants.

The 99 participants were subsequently divided into three groups: those with no diabetic foot, those with uninfected diabetic foot, and those with infected diabetic foot. Each group consisted of 33 participants. Diabetic foot is defined as ulceration occurring distal to the ankle in DM patients (Dietrich et al., 2017). The diabetic foot was further classified as infected or uninfected; an infected diabetic foot presented with classical signs of inflammation, including redness, warmth, swelling, soreness, tenderness, or purulent discharge, and could also include secondary signs such as nonpurulent discharge, friable or discoloured granulation tissue, wound edges erosion, and foul odour (Ahluwalia & Reichert, 2021; Boulton et al., 2018). All participants were assessed for PAD and PN.

Peripheral arterial disease evaluation

PAD was assessed using the ankle-brachial index (ABI) test, which calculates the ratio of the highest systolic blood pressure measured at the dorsalis pedis or posterior tibial artery to the highest systolic pressure recorded in the left or right brachial artery (Lee et al., 2018). The ABI measurement was performed using a handheld Doppler device from Bistos Hi-Bebe Doppler BT-200 L (Seongnam, South Korea) and a sphygmomanometer. Patients were positioned supine for five minutes for the test to ensure accuracy. Systolic blood pressure was first recorded in the brachial arteries of both arms. Subsequently, measurements were taken from the dorsal pedis and posterior tibial arteries, with the cuff positioned just above the ankle. An ABI value of ≤0.90 was used to indicate the presence of PAD (Cicconi, 2024; Hiatt et al., 2021).

Peripheral neuropathy evaluation

PN was evaluated using the Semmes-Weinstein 5.07 (10 g) monofilament test under calm and relaxed conditions (Aithal & Bhat, 2024). Initially, the monofilament tip was applied to the patient's hands to familiarize them with the sensation. The test was then performed by applying the monofilament perpendicularly to the plantar surface of the foot with sufficient pressure to cause the filament to bend or flex. Testing was conducted

at three specific sites on each foot (the first toe, the first and fifth metatarsal heads) while ensuring the patient could not see the application. Each application lasted approximately two seconds per site. PN was diagnosed if the patient could not detect sensation at minimum two of the three sites (Schaper et al., 2016).

Nutritional status

Nutritional status was assessed using the body mass index (BMI) based on the calculation of weight and height. The category of obesity is ≥25.0 kg/m2 (Fajar et al., 2022; Ferdosian et al., 2023; Ikeura et al., 2017).

Hypertension

A diagnosis of hypertension is confirmed at systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, previous diagnosis of hypertension made by a medical doctor or current use of antihypertensive medication (Maulida et al., n.d.; Unger et al., 2020).

Diabetes Mellitus

A Diabetes diagnosis is confirmed by a fasting blood glucose of 126 mg/dL or higher after 8 hours, a postprandial level of 200 mg/dL or more, a glycated hemoglobin of 6.5% or above, or a random glucose reading of 200 mg/dL or greater with hyperglycemic symptoms, alongside a documented history of Diabetes, ongoing antidiabetic medication use, or prior diagnosis by a physician (Jeon et al., 2013; Rhee, 2023).

Statistical analysis

Statistical analysis was conducted using the Chi-square test in SPSS program version 27.0 (Armonk, NY: IBM Corp.), with a significance threshold set at $p<0.05$ for group comparisons.

RESULTS

Characteristics of participants

This study evaluated the prevalence of PAD and PN in three groups of participants: the patients with infected diabetic foot, those with uninfected diabetic foot, and those without diabetic foot. The characteristics of the participants are shown in Table 1.

The mean age of the participants was 57.00±8.99 years, ranging from 29 to 78 years, with the majority (95.45%) being over 40 years old. The duration of DM among the participants ranged from 3 months to 30 years, with a mean of 7.98±5.97 years. Regular DM treatment was reported by 51 patients (51.5%). The study included 56 female participants (56.4%), slightly more than the number of male participants.

Comorbidities assessed in the study included hypertension, obesity, and smoking history. 25.3% of patients were classified as obese, while the remaining 74.7% had a BMI ≤25 kg/m². Additionally, 25 patients (25.3%) had a history of smoking, while 74 patients (74.7%) were non-smokers.

Peripheral arterial disease evaluation

This study assessed the prevalence of PAD across the three groups. The highest prevalence was observed in the infected diabetic foot group (84.8%), followed by the uninfected diabetic foot group (66.7%), and the group with no diabetic foot (15.2%) (Table 2). Statistical analysis revealed a significant difference between the groups ($p<0.001$).

Peripheral neuropathy evaluation

The evaluation of PN prevalence among the study groups was also presented in Table 2. The infected diabetic foot group showed the highest PN prevalence at 93.9%, followed by the uninfected diabetic foot group at 84.8% and the group without diabetic foot at 42.4%. Consistent with the findings for PAD, these differences were statistically significant ($p < 0.001$).

Peripheral arterial disease and peripheral neuropathy coexistence evaluation

The concurrence of PAD and PN across the groups was analyzed (Table 3). The analysis categorized participants into four groups: no PAD and no PN, PN without PAD, PAD without PN, and the presence of both PAD and PN. In the infected diabetic foot group, 78.8% of participants had both PAD and PN, while none were free of both conditions. Among the uninfected diabetic foot group, 54.5% exhibited both conditions, 12.1% had only PAD, 30.3% had only PN, and 3% had neither condition. In the group without diabetic foot, only 6.1% had both PAD and PN, with the majority (48.5%) having neither condition. Statistical analysis confirmed that these differences were significant ($p < 0.001$).

DISCUSSION

Infected diabetic foot represents one of the most severe complications in individuals with DM. Contributing factors include PAD and PN, among others (Meena & C., 2019). This study involved 99 participants whose characteristics were assessed based on age, sex, duration of DM, treatment adherence, hypertension, nutritional status, and smoking history. Hemoglobin A1c (HbA1c) was intended to be included in the study characteristics. However, due to a high prevalence of anemia among the participants, complete HbA1c data could not be obtained. Statistical analysis of these characteristics revealed no significant differences ($p>0.05$) across the three subject groups (no diabetic foot, uninfected diabetic foot, and infected diabetic foot).

This study found significant differences in the prevalence of PAD among the three patient groups ($p<0.001$). These findings align with research conducted in Saudi Arabia, which reported that PAD was present in 33.1% of patients with DFU (Altoijry et al., 2021). Similarly, a study by Tressiera-Ayala and Garcia Rojas identified PAD as a significant factor associated with DFU ($p<0.001$), with 78% of patients affected by DFU also experiencing PAD (Tresierra-Ayala & García Rojas, 2017). Additionally, research by Hao et al. demonstrated a higher prevalence of diabetic foot infections among patients with PAD compared to those without PAD (Hao et al., 2014). However, accurately determining the prevalence of PAD using ABI is challenging due to its limitations. Normal ABI values do not entirely exclude the possibility of PAD, particularly in diabetic patients, where arterial sclerosis may yield falsely normal results. Nevertheless, a low ABI is a reliable indicator of PAD when detected.

The results of the monofilament test used to assess PN across the three groups demonstrated statistically significant findings ($p<0.001$), indicating a strong correlation between PN and infected diabetic foot. This study revealed that neuropathy was present in over 80% of patients with diabetic foot conditions: 84.8% in those without infection and 93.9% in those with infected diabetic foot. Similar findings were reported by Mshelia-Reng et al. where 835 out of 1040 patients (80.1%) with diabetic foot exhibited neuropathy (Mshelia-Reng et al., 2022). Additionally, Meloni et al., in their study of 1,198 diabetic foot patients, reported that 92% experienced PN (Meloni et al., 2020). Research by Aliyu et al. further supported these results, showing that 49 out of 57 patients with DFU had neuropathy (Aliyu et al., 2023). To date, no studies have specifically analyzed the association between neuropathy and infected diabetic foot.

This study also evaluated the prevalence of coexisting PAD and PN in patients with infected diabetic foot. It was found that 78.8% of patients with infected diabetic foot had both PAD and PN, compared to only 6.1% of patients without diabetic foot with this concurrence ($p<0.001$). To the best of our knowledge, this study is the first to analyze the coexistence of these conditions in patients with infected diabetic foot. A related study conducted by Sangeetha and Manikan reported that the prevalence of both PAD and PN in diabetic patients was 13%, while 87% of the patients did not have these conditions. Notably, the diabetic patients included in their study did not present with diabetic foot (Meena & C., 2019).

The study has several strengths that contribute to its significance in understanding the prevalence of PAD and PN in individuals with infected diabetic foot. Firstly, the study's comprehensive nature is a strength as it delves into the prevalence of these conditions in a specific population, providing valuable insights into the interaction of PAD and PN in the

context of diabetic foot infections. Additionally, the study utilized a well-defined methodology, including standardized assessments for PAD and PN. The ankle-brachial index test and the Semmes-Weinstein monofilament test are widely accepted and validated methods for evaluating these conditions, enhancing the reliability and validity of the study's findings.

The study has several limitations. Firstly, the study sample was relatively small, consisting of 99 participants from a specific geographical area, which may limit the generalizability of the findings to other populations. Furthermore, the study did not include HbA1c data due to a high prevalence of anemia among the participants, which could have provided valuable insight into the relationship between glycemic control and the prevalence of diabetic foot complications. Lastly, the study did not explore potential confounding variables such as socioeconomic status, access to healthcare, and specific diabetes management regimens, which could have influenced the prevalence of PAD and PN in the study participants.

CONCLUSION

The infected diabetic foot showed the highest prevalence of PAD and PN compared to both uninfected diabetic foot and non-diabetic foot cases.

Conflict of interest: none declared

Author's contributions: APH, HU, and IM drafted the manuscript. HU, SB and HR designed and concepted the study. APH and AAZ collected and analyzed and interpreted the data. IM, HR, and SB revised manuscript critically for important intellectual content. All authors participated in the final draft preparation, manuscript revision, and critical evaluation of the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

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Informed consent: informed consent was obtained from all participants in the study.

Ethics approval and consent to participate: This study has been approved by the Research Ethics Committee of the Faculty of Medicine, Hasanuddin University through the publication of an ethical approval letter number 627/UN4.6.4.5.31/PP36/2024. The

study adhered to the ethical principles, ensuring the protection of participants' rights and confidentiality.

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TABLES

Table 1. Characteristics of participants

Variable	Group			*p*-value*
	No diabetic foot	Uninfected diabetic foot	Infected diabetic foot	
Age (years)	58.48±11.38	56.70±7.09	55.82±8.02	0.386
Sex				
Male (n, %)	15 (45.50)	14 (42.40)	14 (42.40)	0.960
Female (n, %)	18 (54.50)	19 (57.60)	19 (57.60)	
Nutritional status				
Non-obesity (n, %)	28 (84.80)	23 (69.70)	23 (69.70)	0.262
Obesity (n, %)	5 (15.20)	10 (30.30)	10 (30.30)	
Hypertension				
Yes (n, %)	20 (60.60)	20 (60.60)	12 (36.40)	0.075
No (n, %)	13 (39.40)	13 (39.40)	21 (63.60)	
History of smoking				
Yes (n, %)	10 (30.30)	8 (24.20)	7 (21.20)	0.385
No (n, %)	23 (69.70)	25 (75.80)	26 (78.80)	
DM duration (years)	9.00±6.19	7.85±6.17	7.09±5.56	0.297
Adherence to treatment				
Yes (n, %)	17 (51.50)	16 (48.50)	18 (54.50)	0.886
No (n, %)	16 (48.50)	17 (51.50)	15 (45.50)	

Abbreviation: DM, diabetes mellitus; *Chi-square test

Table 2. Prevalence of peripheral arterial disease and peripheral neuropathy in diabetes mellitus patients with no diabetic foot, with uninfected diabetic foot, and with infected diabetic foot

Variable	No diabetic foot (n, %)	Uninfected diabetic foot (n, %)	Infected diabetic foot (n, %)	*p*-value*
PAD				
Yes	5 (15.2)	22 (66.7)	28 (84.8)	<0.001
No	28 (84.8)	11 (33.3)	5 (15.2)	
PN				
Yes	14 (42.4)	28 (84.8)	31 (93.9)	<0.001
No	19 (57.6)	5 (15.2)	2 (6.1)	

Abbreviation: PAD, peripheral arterial disease; PN, peripheral neuropathy; *Chi-square test.

Table 3. Prevalence of coexistence of peripheral arterial disease and peripheral neuropathy in diabetes mellitus patients with no diabetic foot, with uninfected diabetic foot, and with infected diabetic foot

Variable	No diabetic foot (n, %)	Uninfected diabetic foot (n, %)	Infected diabetic foot (n, %)	*p*-value*
No PAD and no PN	16 (48.5)	1 (3.0)	0 (0.0)	
PN without PAD	12 (36.4)	10 (30.3)	5 (15.2)	<0.001
PAD without PN	3 (9.1)	4 (12.1)	2 (6.1)	
Both PAD and PN	2 (6.1)	18 (54.5)	26 (78.8)	

Abbreviation: PAD, peripheral arterial disease; PN, peripheral neuropathy; *Chi-square test.