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Frequency of Risk Factor in Peripheral Arterial Disease in Diabetes

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ABSTRACT

Background: *Peripheral arterial disease (PAD) is a common yet frequently under-recognized macrovascular complication of type 2 diabetes mellitus (T2DM) that increases risk of lower-limb morbidity and adverse cardiovascular outcomes. Objective, reproducible screening using the ankle–brachial index (ABI) can identify PAD, including asymptomatic disease, and may facilitate targeted risk-factor modification.* ***Objective:*** *To determine the prevalence of ABI-defined PAD and evaluate the frequency and association of key risk factors among adults with T2DM.* ***Methods:*** *This cross-sectional observational study was conducted in the Department of Medicine, Sandeman Provincial Hospital, Quetta, from January 6 to June 6, 2025. Adults (≥18 years) with T2DM of ≥6 months' duration were enrolled. ABI was measured using a handheld Doppler ultrasound device; PAD was defined as ABI ≤0.9. Demographic and clinical variables including BMI, HbA1c, hypertension, smoking history, and family history of diabetes were recorded. Associations with PAD were tested using chi-square and t-tests, with crude odds ratios (ORs) and 95% confidence intervals (CIs) calculated; Pearson correlation assessed relationships with ABI.* ***Results:*** *Among 897 participants (56.5% female), mean age was 50.68±11.65 years and mean BMI 26.29±5.49 kg/m²; 68.7% had BMI ≥23 kg/m², 27.9% had hypertension, and 7.7% reported smoking. Mean ABI was 1.11±0.17 and PAD prevalence was 10.0% (90/897). PAD was associated with BMI ≥23 kg/m² (OR 2.68, 95% CI 1.49–4.83; p=0.001), hypertension (OR 1.85, 95% CI 1.18–2.90; p=0.007), and smoking (OR 3.08, 95% CI 1.68–5.66; p<0.001). HbA1c showed a weak inverse correlation with ABI (r=−0.070; p=0.036).* ***Conclusion:*** *ABI-defined PAD affected one in ten adults with T2DM and was strongly associated with obesity, hypertension, and smoking, supporting targeted ABI screening and aggressive risk-factor control in high-risk subgroups.*

Keywords*: ankle–brachial index; hypertension; peripheral arterial disease; smoking; type 2 diabetes mellitus.*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a rapidly expanding global health challenge. The International Diabetes Federation estimates that 463 million adults were living with diabetes in 2019, with projections rising to approximately 700 million by 2045, underscoring the scale of current and future cardiometabolic burden (1). Pakistan is among the countries facing a particularly high and growing burden, with population-based estimates suggesting that roughly 17% of adults have diabetes or dysglycemia, creating a large at-risk pool for vascular complications and their downstream disability and costs (2). Within this landscape, peripheral arterial disease (PAD) represents a clinically consequential yet frequently under-recognized complication of diabetes, contributing to diabetic foot morbidity, lower-limb ulceration, and preventable amputations, as well as broader cardiovascular risk (3).

PAD is classically characterized by atherosclerotic narrowing or occlusion of arteries supplying the lower extremities, resulting in impaired perfusion and ischemic tissue vulnerability (4). Globally, PAD affects more than 200 million people and contributes materially to years lived with disability and vascular mortality, with substantial heterogeneity across regions driven by risk-factor distribution, healthcare access, and case-finding practices (5). A major clinical challenge is that PAD is often clinically silent: fewer than one in five

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individuals present with typical claudication symptoms, and symptom-based detection therefore underestimates true burden (6). In patients with T2DM, concurrent peripheral neuropathy can further mask ischemic symptoms, shifting detection toward objective screening tools and strengthening the case for routine vascular assessment in high-risk subgroups (7).

The ankle–brachial index (ABI) is a simple, non-invasive measure with established prognostic relevance: lower ABI values are inversely associated with incident cardiovascular and cerebrovascular events and with adverse outcomes, making ABI both a diagnostic and risk-stratification instrument in clinical and epidemiologic settings (8). Low ABI is consistently linked with traditional and diabetes-related vascular risk factors, including diabetes itself, hypertension, dyslipidemia, smoking, and chronic kidney disease (9,10). Beyond these conventional determinants, inflammatory pathways also appear to play a role in PAD pathobiology; biomarkers such as C-reactive protein, interleukin-6, and homocysteine have been associated with PAD presence and severity, reinforcing the concept of PAD as a systemic atherosclerotic phenotype rather than an isolated limb condition (11). Despite the mechanistic coherence of these associations, observed PAD prevalence and risk-factor profiles vary widely across studies because of differences in patient selection, comorbidity burden, and diagnostic thresholds (e.g., ABI cutoffs), which complicates direct generalization across settings.

In Pakistan, available evidence indicates that PAD among T2DM patients may be common, but local estimates are inconsistent and appear sensitive to methods and population characteristics. For example, one study from Karachi reported a PAD prevalence of 29% in T2DM patients, illustrating a potentially substantial burden when systematically assessed (12). However, the evidence base remains geographically uneven, and there is limited contemporary data from Baluchistan—particularly from tertiary-care settings in Quetta—where patterns of obesity, hypertension, tobacco exposure, and glycemic control may differ, and where late presentation for complications could amplify clinical impact. This yields a practical knowledge gap: clinicians and health systems require setting-specific estimates of ABI-defined PAD prevalence and a clear understanding of how common, modifiable risk factors (such as elevated BMI, hypertension, and smoking) are distributed among patients with and without PAD to inform screening intensity, prevention counseling, and resource allocation.

Accordingly, the present study addresses the following research objective framed in a PICO-aligned structure: among adults with T2DM (Population), do common modifiable risk factors—particularly elevated body mass index, hypertension, smoking history, and poor glycemic control (Exposures)—compared with absence of these risk factors (Comparator)—associate with a higher frequency of ABI-defined PAD (Outcome, PAD defined as ABI ≤0.9), and what is the prevalence of PAD in this population.

MATERIAL AND METHODS

This cross-sectional observational study was conducted to estimate the prevalence of peripheral arterial disease (PAD) and to evaluate its association with selected cardiovascular risk factors among adults with type 2 diabetes mellitus (T2DM), following internationally accepted reporting standards for observational research (13). The study was carried out in the Department of Medicine at Sandeman Provincial Hospital, Quetta, a major tertiary-care referral center serving urban and rural populations of Baluchistan, Pakistan. Data collection took place over a six-month period from January 6, 2025, to June 6, 2025, allowing for

adequate participant accrual and standardized assessment procedures across the study interval.

Eligible participants included adults of either sex aged 18 years or older with a confirmed diagnosis of T2DM and a minimum disease duration of six months, ensuring sufficient exposure time for the potential development of vascular complications. Patients with type 1 diabetes mellitus were excluded to maintain etiologic homogeneity. Additional exclusion criteria included refusal to provide informed consent, current use of vasodilator medications that could influence peripheral vascular tone and ABI measurements, and end-stage renal disease requiring dialysis, given its independent and strong association with vascular calcification and altered ABI values. Participants were selected using a consecutive sampling approach from patients attending medical outpatient clinics and inpatient medical wards during the study period, minimizing selection bias within the hospital-based population.

All eligible patients were approached by trained study personnel, and written informed consent was obtained prior to enrollment. Data collection was performed using a structured proforma designed to ensure uniform capture of demographic, clinical, and anthropometric variables. Age and sex were recorded as reported by the participant. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, with obesity operationally defined using an Asian-specific cutoff of BMI $\geq$23 kg/m^2 to reflect regional cardiometabolic risk profiles. Blood pressure was measured using a calibrated sphygmomanometer after the participant had rested in a seated position, and hypertension was defined as a prior physician diagnosis or documented use of antihypertensive medication. Smoking status was recorded based on patient self-report and categorized as a positive history if the participant reported current or past cigarette smoking. Glycemic control was assessed using the most recent glycated hemoglobin (HbA1c) value, dichotomized at 7% in accordance with widely used clinical thresholds for adequate control.

The primary outcome, PAD, was assessed using the ankle–brachial index (ABI), a validated and non-invasive measure of lower-extremity arterial perfusion with established diagnostic and prognostic utility (14). ABI measurements were performed by trained clinicians using a handheld Doppler ultrasound device with the participant in the supine position after an adequate rest period.

Systolic blood pressures were obtained from both brachial arteries and from the dorsalis pedis and posterior tibial arteries in each ankle. For each leg, the ABI was calculated as the ratio of the highest ankle systolic pressure to the corresponding brachial systolic pressure. The lower ABI value from the two legs was used for analysis to avoid underestimation of disease severity. PAD was defined a priori as an ABI value of $\leq$0.9, consistent with established diagnostic criteria (15).

Several steps were undertaken to enhance internal validity and reproducibility. Standardized measurement protocols were used for anthropometric, blood pressure, and ABI assessments, and all data collectors received uniform training before study initiation. Clear operational definitions were applied consistently across participants to reduce information bias. Potential confounding by age, sex, glycemic control, hypertension, BMI, and smoking was addressed through stratified analyses and correlation testing, acknowledging the limitations inherent to the cross-sectional design.

Sample size estimation was performed prior to study initiation using an anticipated PAD prevalence of approximately 29% among patients with T2DM, based on prior regional data, with a 95% confidence level and a margin of error of 3%, yielding a required sample size of 879 participants. To account for potential non-response and incomplete data, a slightly larger

number of participants were recruited. All collected data were checked for completeness and consistency prior to analysis to ensure data integrity.

Statistical analysis was conducted using IBM SPSS Statistics version 26.0. Continuous variables were summarized as means with standard deviations, while categorical variables were presented as frequencies and percentages. Comparisons between participants with and without PAD were performed using the independent sample t-test for continuous variables and the chi-square test for categorical variables. Pearson correlation analysis was applied to assess the relationship between ABI values and continuous variables such as age and HbA1c. A p-value of less than 0.05 was considered statistically significant. Missing data were minimal and handled by complete-case analysis to preserve interpretability.

The study protocol was reviewed and approved by the Institutional Ethical Committee of Sandeman Provincial Hospital, Quetta. All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, and confidentiality of participant information was maintained throughout the study by anonymizing data prior to analysis.

RESULTS

Table 1 summarizes the baseline profile of the 897 adults with T2DM included in the analysis. Women comprised 507 participants (56.5%) and men 390 (43.5%). The cohort was predominantly middle-aged: 446 patients (49.7%) were 46–60 years old, 274 (30.5%) were 31–45 years, 143 (15.9%) were older than 60 years, and 34 (3.8%) were 18–30 years. The mean age was 50.68 ± 11.65 years and the mean BMI was 26.29 ± 5.49 kg/m².

Using the Asian BMI threshold, 616 patients (68.7%) had BMI ≥23 kg/m², while 281 (31.3%) were <23 kg/m². Glycemic control was suboptimal in most participants: 695 (77.5%) had HbA1c ≥7% and only 202 (22.5%) had HbA1c ≤7%. Hypertension was present in 250 patients (27.9%), a family history of diabetes was reported by 126 (14.0%), and 69 participants (7.7%) reported a history of smoking.

Table 2 presents PAD status across the same variables and quantifies key associations. Overall, PAD (ABI ≤0.9) was identified in 90 participants, yielding a prevalence of 10.0%, while 807 (90.0%) did not meet the PAD criterion. Sex showed a borderline distributional difference: among PAD cases, 59 were female (65.6%) and 31 were male (34.4%), whereas among non-PAD participants, 448 were female (55.5%) and 359 male (44.5%), but this did not reach statistical significance (p=0.068).

Age categories also did not show a statistically significant association with PAD (p=0.136), although PAD cases were numerically concentrated in the 46–60 group (47/90, 52.2%) and the >60 group (19/90, 21.1%), compared with 399/807 (49.4%) and 124/807 (15.4%) in the non-PAD group, respectively.

In contrast, BMI, hypertension, and smoking were clearly associated with PAD. For BMI, 76 of 90 PAD cases (84.5%) had BMI ≥23 kg/m² compared with 540 of 807 non-PAD participants (66.9%), while only 14 PAD cases (15.5%) were in the BMI <23 category versus 267 non-PAD participants (33.1%). This corresponded to nearly threefold higher crude odds of PAD in BMI ≥23 kg/m² (OR 2.68, 95% CI 1.49–4.83; p=0.001). Hypertension was present in 36 PAD cases (40.0%) compared with 214 non-PAD participants (26.5%), indicating higher PAD burden among hypertensive patients (OR 1.85, 95% CI 1.18–2.90; p=0.007). Smoking history showed the strongest association: 16 PAD cases (17.8%) reported smoking versus 53 non-PAD participants (6.6%), translating into approximately threefold increased odds of PAD among smokers (OR 3.08, 95% CI 1.68–5.66; p<0.001).

Table 1. Baseline Characteristics of Study Participants (n = 897)

Characteristic	Category	n (%)
Sex	**Male**	**390 (43.5)**
	Female	**507 (56.5)**
Age (years)	18–30	34 (3.8)
	31–45	274 (30.5)
	46–60	446 (49.7)
	>60	143 (15.9)
BMI (kg/m²)	<23	281 (31.3)
	≥23	616 (68.7)
HbA1c (%)	≤7	202 (22.5)
	≥7	695 (77.5)
Hypertension	Yes	250 (27.9)
Family history of diabetes	Yes	126 (14.0)
History of smoking	Yes	69 (7.7)

Table 2. Association of Peripheral Arterial Disease (PAD) With Study Variables (n = 897)

Variable	PAD Yes n (%)	PAD No n (%)	p-value	Crude OR (95% CI)
Sex			**0.068**	**—**
Male	31 (34.4)	359 (44.5)		
Female	59 (65.6)	448 (55.5)		
Age (years)			0.136	—
18–30	5 (5.6)	29 (3.6)		
31–45	19 (21.1)	255 (31.6)		
46–60	47 (52.2)	399 (49.4)		
>60	19 (21.1)	124 (15.4)		
BMI (kg/m²)			0.001	2.68 (1.49–4.83)
<23	14 (15.5)	267 (33.1)		
≥23	76 (84.5)	540 (66.9)		
HbA1c (%)			0.053	1.81 (0.97–3.36)
≤7	13 (14.4)	189 (23.4)		
≥7	77 (85.6)	618 (76.6)		
Hypertension	36 (40.0)	214 (26.5)	0.007	1.85 (1.18–2.90)
Family history of diabetes	18 (20.0)	108 (13.4)	0.087	1.61 (0.92–2.82)
History of smoking	16 (17.8)	53 (6.6)	<0.001	3.08 (1.68–5.66)

HbA1c category showed a near-threshold pattern but did not meet conventional statistical significance in categorical comparison. Among PAD cases, 77/90 (85.6%) had HbA1c ≥7% versus 618/807 (76.6%) in the non-PAD group, while HbA1c ≤7% was seen in 13/90 PAD cases (14.4%) compared with 189/807 non-PAD participants (23.4%) (p=0.053). The corresponding

crude odds ratio suggested higher PAD odds with HbA1c ≥7% (OR 1.81, 95% CI 0.97–3.36), but with uncertainty spanning the null. Family history of diabetes also did not show a statistically significant relationship with PAD: 18/90 PAD cases (20.0%) reported family history compared with 108/807 non-PAD participants (13.4%) (p=0.087), with a modest and imprecise elevation in odds (OR 1.61, 95% CI 0.92–2.82).

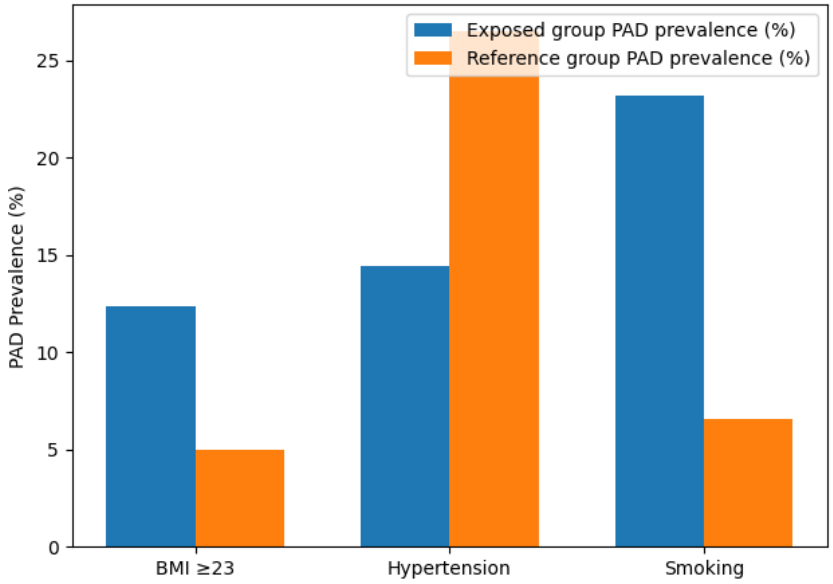

Figure 1 Gradient of PAD Prevalence Across Key Modifiable Risk Factors in T2DM

The figure illustrates a clear exposure–outcome gradient in ABI-defined peripheral arterial disease (PAD) prevalence across three clinically actionable risk factors. PAD prevalence among participants with BMI ≥23 kg/m² was approximately 12.3%, compared with 5.0% among those with BMI <23 kg/m², demonstrating more than a twofold excess burden in overweight and obese patients. A similar gradient was observed for hypertension, where PAD prevalence reached 14.4% among hypertensive individuals versus 6.6% in normotensive participants, reinforcing hypertension as a key vascular amplifier in diabetes. The steepest differential was seen with smoking exposure: PAD prevalence among smokers was 23.2%, compared with 6.6% among non-smokers, highlighting a more than threefold relative increase. Collectively, these gradients visually emphasize a dose–response–like pattern across modifiable risk factors, underscoring the disproportionate vascular burden borne by smokers, hypertensive patients, and those with elevated BMI within the T2DM population, and reinforcing the clinical value of targeted ABI screening and aggressive risk-factor modification in these subgroups.

DISCUSSION

In this cross-sectional study of adults with type 2 diabetes mellitus (T2DM) attending a tertiary-care hospital in Quetta, peripheral arterial disease (PAD), defined by an ankle–brachial index (ABI) ≤0.9, was identified in 10% of participants. This finding confirms that PAD represents a substantial and clinically relevant burden among individuals with T2DM, even in the absence of overt symptoms, and supports the growing recognition of PAD as a frequent yet underdiagnosed manifestation of systemic atherosclerosis in diabetic populations (16). Although the observed prevalence is lower than that reported in several regional and international studies, it remains considerably higher than estimates in the general population, underscoring the amplifying role of diabetes in peripheral vascular disease risk (17). The PAD prevalence observed in the present study is lower than figures reported from Karachi (29%) and Lahore (31–41%), as well as studies from Brazil and sub-Saharan Africa reporting prevalence rates exceeding 20% (12,14,15,18). Several factors may

account for this variation, including differences in population characteristics, duration and severity of diabetes, coexisting cardiovascular risk factors, and, importantly, methodological heterogeneity such as ABI thresholds used to define PAD. Studies employing more permissive cutoffs (e.g., ABI <1.0) have consistently reported higher prevalence estimates, which limits direct comparability and highlights the importance of standardized diagnostic criteria when interpreting epidemiological data (19). The use of ABI ≤0.9 in the present study aligns with widely accepted diagnostic standards and strengthens the specificity of PAD detection (20).

A key finding of this study is the strong association between PAD and modifiable cardiovascular risk factors, particularly elevated body mass index (BMI), hypertension, and smoking. Participants with BMI ≥23 kg/m² demonstrated nearly threefold higher odds of PAD compared with those below this threshold, reinforcing the role of adiposity in accelerating atherosclerotic processes in diabetes. Obesity promotes endothelial dysfunction, insulin resistance, and chronic inflammation, all of which contribute to macrovascular disease progression (21). The use of an Asian-specific BMI cutoff is particularly relevant in South Asian populations, where cardiometabolic risk manifests at lower BMI levels than in Western populations.

Hypertension was also significantly associated with PAD, with hypertensive patients exhibiting almost twice the odds of PAD compared with normotensive individuals. This finding is consistent with prior studies identifying hypertension as an independent predictor of PAD in diabetic cohorts, likely mediated through increased arterial stiffness, endothelial injury, and accelerated plaque formation (22). From a clinical standpoint, this reinforces the importance of stringent blood pressure control not only for coronary and cerebrovascular protection but also for preservation of lower-limb perfusion in patients with diabetes.

Smoking emerged as the strongest risk factor in this cohort, with smokers demonstrating more than threefold higher odds of PAD compared with non-smokers. This pronounced association mirrors findings from regional and international studies and reflects the potent pro-atherogenic effects of tobacco exposure, including oxidative stress, inflammation, and direct endothelial toxicity (23). The steep gradient in PAD prevalence among smokers underscores smoking cessation as a critical and high-yield intervention for reducing limb-related morbidity in T2DM.

Although categorical analysis of glycemic control did not reach statistical significance, a weak but statistically significant inverse correlation between HbA1c and ABI was observed, suggesting that poorer glycemic control is associated with lower ABI values. This aligns with evidence indicating that chronic hyperglycemia contributes to vascular damage through advanced glycation end products, oxidative stress, and microvascular dysfunction, which may indirectly exacerbate macrovascular disease (24). The modest strength of this association may reflect the multifactorial nature of PAD and the cross-sectional design, which limits assessment of cumulative glycemic exposure over time.

Several limitations should be considered when interpreting these findings. The cross-sectional design precludes causal inference and limits the ability to establish temporal relationships between risk factors and PAD development. The study was conducted at a single tertiary-care center, which may restrict generalizability to community-based populations. Additionally, data on duration of diabetes, lipid profiles, and renal function short of dialysis were not incorporated, which may have resulted in residual confounding. Despite these limitations, the study's strengths include a relatively large sample size, standardized ABI assessment, and focused evaluation of clinically modifiable risk factors relevant to routine practice.

CONCLUSION

In conclusion, this study demonstrates that peripheral arterial disease affects one in ten adults with type 2 diabetes mellitus in a tertiary-care setting in Quetta, Pakistan, and is strongly associated with modifiable risk factors, particularly elevated body mass index, hypertension, and smoking. These findings support the incorporation of targeted ABI screening and aggressive risk-factor modification strategies into routine diabetes care to enable earlier identification of PAD and reduce the risk of limb-related and cardiovascular complications.

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DECLARATIONS

Ethical Approval: Ethical approval was by institutional review board of Respective Institute.

Informed Consent: Informed Consent was taken from participants.

Authors' Contributions:

Concept: SS; Design: J; Data Collection: MU; Analysis: AK; Drafting: MK

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