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Original Article

Subclinical lower limb Peripheral Arterial Disease in Patients with Type 2 Diabetes Mellitus: A cross-sectional study.

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Abstract

Background: Peripheral artery disease (PAD) is highly prevalent in patients with diabetes mellitus. The ankle-brachial index (ABI) measurement is used to diagnose peripheral arterial disease, and little is known about its prevalence in asymptomatic type 2 Diabetic patients. This study aimed to determine the prevalence of subclinical peripheral artery disease in patients with type II diabetes mellitus.

Methodology: It was a descriptive study conducted at the Peshawar Institute of Medical Sciences, from Feb 2022 to Aug 2022. Two hundred sixty-four patients with type II diabetes (for more than three years) with no clinical features of peripheral arterial disease were assessed by measuring ankle brachial pressure index for subclinical peripheral arterial disease. Reading less than 0.9 was positive for peripheral artery disease in the lower limbs.

Results: Peripheral Arterial Disease was present in 115 (43.6%) patients and absent in 149 (56.4%) patients. The peripheral artery disease was significantly more in males, those with age greater than 55 years, smokers, and hypertensive patients ($p\text{-value} \leq 0.05$) but was not associated with the duration of diabetes or BMI of the patient ($p\text{-value} > 0.05$)

Conclusion: There was a high prevalence of asymptomatic peripheral artery disease in Type 2 Diabetic patients using ankle-brachial pressure index measurement. Those with ages greater than 55 years, smokers, hypertensive, and males were particularly at higher risk.

Keywords

Type II Diabetes Mellitus, Peripheral artery disease, Ankle Brachial Pressure index.



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Introduction

We have a diabetes mellitus pandemic, and more than 170 million people across the globe suffer from diabetes mellitus (DM), with projected figures of 366 million by 2030¹. Peripheral arterial disease (PAD) is one of the major macrovascular complications of type 2 DM that contributes significantly to diabetes-related morbidity and mortality². It is characterized by stenosis or occlusion of arteries, mainly affecting lower limbs due to atherosclerosis. Studies have linked the rise in PAD incidence to diabetes, which is associated with a higher risk of atherosclerosis³. The incidence of PAD is two to fourfold in the diabetic population, with a prevalence of 9.5% in patients older than 40 years compared to 4.5% in the non-diabetic group⁴.

PAD has a chronic and predominantly asymptomatic course in patients having Diabetes Mellitus. Between 9% and 23% of people older than 55 years are affected by PAD, but only a minor percentage (10%) of the individual will present with the classical disease findings. Diabetes and PAD increase the risk of amputation significantly, and both can be asymptomatic in the initial course of the disease. Ankle Brachial Pressure index can be calculated in outpatients or bedside and is a simple and safe screening tool for both symptomatic and asymptomatic PAD⁵.

Peripheral arterial disease in diabetic patients has been documented in different studies conducted worldwide. Still, the true prevalence of PAD has been difficult to determine because of its asymptomatic nature at an early stage. Despite being a known complication of diabetes, PAD remains underdiagnosed till the late stage. Early identification of PAD at the subclinical stage in diabetic patients may help preventive design strategies and possible early interventions to prevent associated morbidity and mortality. Furthermore, it can also indicate Cardiovascular and cerebrovascular-related risks in these patients at an early stage. International and local literature is available that looks into the disease burden of PAD in diabetic patients⁶⁻⁹. Still, most have included all diabetic patients without considering

the presence or absence of clinical features of peripheral arterial disease. We mainly focused on finding PAD prevalence in the lower limbs of diabetic patients at the subclinical stage. This will depict its burden at an early stage and may help in the early prevention and treatment of peripheral arterial disease & associated complications.

Methodology

This observational cross-sectional study was conducted at the Peshawar Institute of Medical Sciences, Peshawar, after obtaining approval from the institutional ethical committee and informed consent was taken from all the study participants. The study duration was six months and was conducted from 12th Feb to 11th Aug 2022. Patients diagnosed with type 2 diabetes for at least three years duration, age group between 40-70 years with either gender, were included in the study. Patients were clinically assessed for symptoms and signs of peripheral arterial disease. Any patient having a prior diagnosis of peripheral arterial disease, history of intermittent claudication, leg ulcer, gangrene, coronary stenting, or ischemic heart disease was excluded from the study. We also excluded patients with a history of vasculitis, previous trauma to the arterial vasculature, diminished lower limb peripheral pulses, or any arterial graft procedures known from patient history and records. The sample size was taken 264, keeping the prevalence of PAD in diabetic patients at 22% based on a previous study¹¹, with a confidence interval 95% and a margin of error of 5% using the WHO sample size calculator.

Demographics like the name, age, and gender of the participants were noted. Clinical assessment was done with detailed patient history and physical examination. Fasting/Random blood sugar, hypertension, BMI, smoking status, and presence of peripheral pulses in lower limbs (Popliteal, Dorsalis pedis, and Posterior tibial) were recorded on pre-designed proforma. Any patient who had any feature as per our exclusion criteria was excluded from the study. Ankle Brachial Pressure Index (ABI) was taken by measuring the systolic blood pressure from the Brachial arteries of both arms and the Dorsalis pedis and posterior tibial

arteries of both legs. These measurements were taken after resting the patient in a supine position for 10 minutes. We measured the pressures with the right arm, the right leg, the left leg, and the left arm. Readings were taken with blood pressure cuffs applied to the patient's arm and lower calf (above the cubital fossa and ankle). Systolic pressure readings were recorded with a standard hand-held doppler. Both arm pressure readings were taken, and the higher blood pressure was used to calculate ABI. For both the ankle pressure measurements (posterior tibial and dorsalis pedis arteries), the higher pressure was used to calculate the ABI of the respective side. Sub-clinical PAD was confirmed if any of the ABI values, either right or left, was < 0.90 according to American College of Cardiology/American Heart Association (ACC/AHA) recommendations¹⁰. All these things were done by a single physician having at least two years of clinical experience.

Data collected were analyzed using SPSS version 23.0. Categorical variables such as gender, age groups, smoking status (current smoker with smoking more than six cigarettes per day for at least five years), hypertension (known case of hypertension with at least 1-year duration and on medications), and PAD was expressed as frequencies and proportions. Mean values with standard deviations were calculated for continuous variables such as age, weight, height, BMI, and duration of diabetes. PAD was stratified among age groups, gender, BMI, smoking, hypertension, and duration of diabetes to see the effect modification. Based on WHO-recommended Asian cut-off values for BMI in kg/m^2 ; patients were divided into six groups; underweight ($\text{BMI} < 18.5$), normal ($18.5 - 22.99$), overweight ($23 - 24.99$), mild obesity (class I, $25 - 26.99$), moderate obesity (class II, $27 - 29.99$) and severe obesity (class III, ≥ 30). Post-stratification Chi-square test / Fisher's exact test was used to see the association of these variables on outcome. A p-value of ≤ 0.05 was considered significant.

Results

There were 195(73.9%) males and 69(26.1%) females in our study. There were 155(58.7%) patients who were less than 55 years of age, while 109 (41.3%) patients were equal to or greater than 55 years old. The mean age was 53.82 ± 7.64 , the mean weight was 74.56 ± 8.01 kg, the mean height was 1.49 ± 0.15 meter, and the mean BMI was 25.31 ± 3.84 kg/m^2 . Smoking history was present in 80(30.3%), while it was negative in 184 (69.7%) patients. Hypertension was present in 131 (49.6%), while it was absent in 133 (50.4%) participants. We also stratified our study population according to BMI as follows. 7 (2.7%) were in the underweight category, 69 (26.1%) had normal BMI, 54 (20.5%) were overweight, 50 (18.9%) had mild obesity, 48 (18.2%) had moderate obesity and 36 (13.6%) were having severe obesity. The mean duration of diabetes in our study was 8.90 ± 4.50 years.

The subclinical peripheral arterial disease was present in 115 (43.6%) people, while it was absent in 149 (56.4%) patients. The distribution of peripheral arterial disease according to age, gender, smoking, hypertension, duration of diabetes, and BMI was done as shown in table 2.

In males, 92 (47.2%) showed to be positive for PAD, and this was higher than that of females in whom 23 (33.3%) showed PAD but didn't reach statistical significance ($p=0.044$). Stratification of age showed that patients of age groups greater than 55 had a higher prevalence of PAD (57, 52.3%) when compared to less than 55 years (58, 37.4%). This difference was significant because the p-value was 0.016.

All 80 smokers (100.0%) were positive for PAD in our study. However, in 184 non-smoker patients, 35 (19.0%) had PAD, while 149 (56.4%) had no PAD ($p<0.001$). There was a significant association in patients with hypertension, as 94 (71.8%) had PAD. There was no significant difference in the distribution of peripheral arterial disease in various groups according to BMI ($p=0.360$).

Table 1: Demographic features of the study.

Characteristics		n=264
Gender	Male	195(73.9)
	Female	69(26.1)
Smoking	Yes	80(30.3)
	No	184(69.7)
Hypertension	Yes	131(49.6)
	No	264(50.4)
Age Groups	< 55 Years	155(58.7)
	≥ 55 Years	109(41.3)
PAD	Yes	61(43.6)
	No	203(56.4)
Duration of Diabetes	4-10 years	101(38.3)
	> 10 years	163(61.7)
BMI	Underweight	7(2.7)
	Normal	69(26.1)
	Overweight	54(20.5)
	Mild Obesity (Class-I)	48(18.2)
	Moderate Obesity (Class-II)	50(18.9)
	Severe Obesity (Class-III)	36(13.6)
Age (years)		53.82 ± 7.63
Weight		74.56 ± 8.01
Height		1.48 ± 0.15
BMI (kg/m²)		25.31 ± 3.84
Duration in years		8.91 ± 4.51
Fasting Blood Sugar(mg/dl)		162 ± 17.51
Random Blood sugar(mg/dl)		223 ± 21.31

Categorical variables such as Frequencies and Percentages

Continuous variables as Mean ± Standard deviation.

Table 2: Association with study variables with PAD.

Variables		Subclinical PAD [n(%)]		p-value
		Yes	No	
Gender	Male	92 (47.2)	103 (52.8)	0.044*
	Female	23 (33.3)	46 (66.7)	
Smoking	Yes	80 (100)	-	< 0.001*
	No	35 (19.1)	149 (81.0)	
Age	< 55 years	58 (37.4)	97 (62.6)	0.016*
	≥ 55 years	57 (52.3)	52 (47.7)	
Duration of Diabetes	3-10 years	47 (46.5)	54 (53.0)	0.443
	>10 years	68 (41.7)	95 (58.3)	
Subclinical PAD	Yes	94 (71.8)	37 (28.2)	< 0.001*
	No	21 (15.8)	112 (84.2)	
BMI Groups	Underweight	2 (28.6)	5 (71.4)	0.361
	Normal	29 (42.0)	40 (58.0)	

Overweight	30 (55.6)	24 (44.4)
Mild Obesity (Class-I)	21 (43.8)	27 (56.3)
Severe Obesity (Class-III)	12 (33.3)	24 (66.7)

Categorical variables were presented as Frequencies and Percentages, and Chi-square's / Fisher's exact test was applied. *P-values ≤ 0.05 was considered as significant

Discussion

Peripheral arterial disease is a well-known vascular manifestation of Diabetes mellitus. It is associated with mortality and amputation of the limb, especially in diabetes Mellitus. Coronary artery disease, age, diabetes, hypertension, smoking, and hypercholesterolemia are the risk factors for PAD¹². Peripheral arterial disease can be asymptomatic at the initial stage and can be missed if not actively considered. In our study prevalence of asymptomatic peripheral arterial disease as per ABI in patients who had diabetes mellitus for ≥ 3 years was 43.6% which is significantly high.

Epidemiologic studies propose a strong relationship between diabetes and the prevalence of PAD. Asians are at higher risk for early onset atherosclerosis and cardiovascular disease. They are predisposed to conditions like Diabetes Mellitus and Hyperlipidemia even with lower Body mass index¹³, which was evident from our study. Lower extremity arterial disease is a devastating manifestation of diabetes mellitus and is usually diagnosed later because of late clinical presentation. According to one estimate, 8 % of diabetic patients have peripheral atherosclerosis at diagnosis¹⁴. High prevalence of peripheral arterial disease in patients with Type 2 diabetes mellitus has been shown in a study conducted in Eastern India, where results showed that 53% of patients had asymptomatic mild PAD and 14% had moderate PAD¹⁵. Another study conducted in Natal, Brazil, showed peripheral arterial disease in 13.7% of patients who had Diabetes Mellitus¹⁶. Asymptomatic peripheral arterial disease has been linked with higher cardiovascular mortality and morbidity.

This was shown in a study conducted by Bundo et al., where they found higher coronary and cerebrovascular mortality and morbidity in patients

having asymptomatic peripheral arterial disease¹⁷. Javed et al. conducted a multicenter study at eight focuses all through Pakistan and included 830 patients out of which 262 (31.6%) had PAD, ABI < 0.9 but they did not exclude patients who had clinical features suggestive of Peripheral arterial disease¹⁸.

Furthermore, the prevalence of subclinical peripheral arterial disease was significantly higher in patients having male gender and age greater than 55 years as compared to females and younger patients. Older age and male gender are known cardiovascular risk factors which can lead to peripheral arterial disease and could be the reason for the higher prevalence of peripheral arterial disease in our study¹⁹. A study conducted in Germany in which ABPI was measured showed that the prevalence of PAD was very high in elderly diabetics in comparison to non-diabetic patients²⁰.

A systematic review was done by Alahdab et al. on screening of asymptomatic peripheral arterial disease by measuring ABPI, which also showed a higher prevalence of PAD in patients with diabetes and advanced age²¹. Smoking is a known strong risk factor for atherosclerosis and cardiovascular disease. In our study, all patients who were smokers had the subclinical peripheral arterial disease. Similar results have been founded previously, and the association of peripheral arterial disease has been shown in various studies. Its prevalence increased in patients who are also suffering from Diabetes Mellitus^{22,23}. A meta-analysis by Lu and colleagues also showed a strong association between peripheral arterial disease and cigarette smoking²⁴. In our study, patients with hypertension 94 (71.8%) had PAD. Hypertension has a known association with accelerated atherosclerosis and can lead to early PAD in patients with other risk factors like diabetes and smoking^{25,26}. There was no significant difference in the presence of subclinical

PAD in patients with different BMI in our study. Studies conducted in Brazil²⁵ and USA¹⁹ with many subjects did not show any association of Peripheral arterial disease in Type 2 Diabetic patients with physical activity level or body composition variables, which were consistent with our study results. Though a study conducted by Masood, A. et al. at Mayo hospital Lahore reported an association of peripheral arterial disease with metabolic syndrome²².

There were limitations in our study. Firstly being a cross-sectional study with a limited sample size and time constraints, it would be difficult to estimate the prevalence of asymptomatic PAD in patients with diabetes in the community. Still, it provides local data and emphasizes that clinicians should look for subclinical peripheral arterial disease. Secondly, quantifying smoking is often difficult, and it could have been better to quantify smoking and assess its significance in causing peripheral arterial disease. Though ABI is a simple method, it can give false positive or abnormal results leading to unnecessary intervention, and data for its use in the subclinical setting is insufficient for a general recommendation.

The genuine prevalence of PAD in individuals with diabetes has been hard to determine, particularly when subclinical. It was significantly high in our study and stressed the importance of routine screening of diabetic patients for asymptomatic peripheral arterial disease. Asian ethnicity and late diagnosis of diabetes Mellitus in our setup could be the cause for our findings. Assessment of large-vessel PAD prevalence in patients with clinical features of PAD will dramatically underestimate the true large-vessel PAD prevalence¹⁶. Detection of Peripheral arterial disease at the early subclinical stage can be a double edge sword, as it may be used as a surrogate marker for the prevention of cardiovascular and cerebrovascular diseases and identify patients who need early treatment and intervention, but at the same time may lead to overtreatment and may not prove to be cost-effective.

Given the limitations of relying on the symptoms or clinical signs of PAD, an additional noninvasive test, ABI, can be used to screen patients at an early stage, as it can determine high-risk subjects who can potentially benefit from aggressive atherosclerotic risk reduction. Furthermore, lifestyle interventions at an early stage may lead to a better outcome in terms of cardiovascular morbidity and mortality.

Conclusion

There was a high subclinical peripheral artery disease prevalence in diabetic patients in our study population. Those having an age greater than 55 years, smokers, hypertensive and male gender were having a higher prevalence of PAD. Screening at the initial stage might help identify patients with higher cardiovascular morbidity and mortality who need early treatment. However, the cost-effectiveness of screening asymptomatic patients at the initial stage and the benefit/harm of early intervention needs further studies.

Conflicts of Interest

No potential conflicts of interest were disclosed by the author(s) about the research, authorship, and/or publication of this paper.

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References

1. Armstrong EJ, Waltenberger J, Rogers JH. Percutaneous coronary intervention in patients with diabetes: current concepts and future directions. *J diabetes Sci Technol*. 2014;8(3):581-589.
2. Rhee SY, Kim YS. Peripheral arterial disease in patients with type 2 diabetes mellitus. *Diabetes Metab J*. 2015;39(4):283-290.

3. Guijarro C, Mostaza JM, Hernández-Mijares A. Lower limb arterial disease and renal artery stenosis. *Clinica e Investigacion en Arteriosclerosis: Publicacion Oficial de la Sociedad Espanola de Arteriosclerosis*. 2013;25(5):218-223.
4. Tresierra-Ayala MÁ, Rojas AG. Association between peripheral arterial disease and diabetic foot ulcers in patients with diabetes mellitus type 2. *Medicina Universitaria*. 2017;19(76):123-126.
5. Ali Z, Ahmed SM, Bhutto AR, Chaudhry A, Munir SM. Peripheral artery disease in type II diabetes. *J Coll Physicians Surg Pak*. 2012;22(11):686-689.
6. Soyoye DO, Ikem RT, Kolawole BA, Oluwadiya KS, Bolarinwa RA, Adebayo OJ. Prevalence and correlates of peripheral arterial disease in Nigerians with type 2 diabetes. *Adv Med Sci*. 2016.
7. Oyelade BO, OlaOlorun AD, Amole IO, Odeigah LO, Adediran OS. The prevalence of peripheral arterial disease in diabetic subjects in south-west Nigeria. *Afr J Prim Health Care Fam Med*. 2012;4(1):1-6.
8. Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. *Circulation*. 1985;71(3):510-515.
9. Hiatt WR, Hoag S, Hamman RF. Effect of diagnostic criteria on the prevalence of peripheral arterial disease: the San Luis Valley Diabetes Study. *Circulation*. 1995;91(5):1472-1479.
10. Nativel M, Potier L, Alexandre L, Baillet-Blanco L, Ducasse E, Velho G, Marre M, Roussel R, Rigalleau V, Mohammedi K. Lower extremity arterial disease in patients with diabetes: a contemporary narrative review. *Cardiovasc Diabetol*. 2018;17:1-4.
11. Akram J, Aamir AU, Basit A, Qureshi MS, Mehmood T, Shahid SK, Khoso IA, Ebrahim MA, Omair A. Prevalence of peripheral arterial disease in type 2 diabetics in Pakistan. *JPMA*. 2011;61(7):644.
12. Fowkes FG, Aboyans V, Fowkes FJ, McDermott MM, Sampson UK, Criqui MH. Peripheral artery disease: epidemiology and global perspectives. *Nat Rev Cardiol*. 2017;14(3):156-170.
13. Gadgil MD, Anderson CA, Kandula NR, Kanaya AM. Dietary patterns in Asian Indians in the United States: an analysis of the metabolic syndrome and atherosclerosis in South Asians Living in America study. *J Acad Nutr Diet*. 2014;114(2):238-243.
14. Sales AT, Fregonezi GA, Silva AG, Ribeiro CT, Dourado-Junior ME, Sousa AG, Dias FA. Identification of peripheral arterial disease in diabetic patients and its association with quality of life, physical activity and body composition. *J Vasc Bras*. 2015;14:46-54.
15. Ghosh US, Datta S, Banerjee S. Asymptomatic peripheral arterial disease in type 2 diabetes mellitus: prevalence patterns and risk factor associations. *Int J Diabetes Dev Ctries*. 2011;31:229-238.
16. Zaheer S, Fatima Zeb T, Baloch A, Amin R, Amjad Z, Sheikh A. The multifactorial burden of Type 2 Diabetes mellitus: a study from clinical settings of University Hospital, Karachi, Pakistan. *IJEHSR*. 2020;8(4):275-87.
17. Bundó M, Muñoz L, Pérez C, Montero JJ, Montellà N, Torán P, Pera G. Asymptomatic peripheral arterial disease in type 2 diabetes patients: a 10-year follow-up study of the utility of the ankle brachial index as a prognostic marker of cardiovascular disease. *Ann Vasc Surg*. 2010;24(8):985-993.
18. Makdisse M, Ramos LR, Moreira F, Oliveira A, Berwanger O, Moscardi A, Junqueira V, Rodrigues E, Carvalho AC. A risk score for predicting peripheral arterial disease in individuals 75 years or older. *Arq Bras Cardiol*. 2007;88:630-636.
19. Joosten MM, Pai JK, Bertoia ML, Rimm EB, Spiegelman D, Mittleman MA, Mukamal KJ. Associations between conventional cardiovascular risk factors and risk of peripheral artery disease in men. *Jama*. 2012;308(16):1660-1667.
20. Lange S, Diehm C, Darius H, Haberl R, Allenberg JR, Pittrow D, Schuster A, Von Stritzky B, Tepohl G, Trampisch HJ. High prevalence of peripheral arterial disease and low treatment rates in elderly primary care patients with diabetes. *Exp Clin Endocrinol Diabetes*. 2004;112(10):566-573.
21. Alahdab F, Wang AT, Elraiyah TA, Malgor RD, Rizvi AZ, Lane MA, Prokop LJ, Montori VM, Conte MS, Murad MH. A systematic review for the screening for peripheral arterial disease in asymptomatic patients. *J Vasc Surg Cases*. 2015;61(3):42S-53S.
22. Masood A, Saleem K, Khawaja A, Amin M, Mirza M, Butt S, et al. Frequency of Asymptomatic Peripheral Disease in Patients of Metabolic Syndrome. *Pak J Med Health Sci*. 2012;6(3):632-636.
23. Eraso LH, Fukaya E, Mohler III ER, Xie D, Sha D, Berger JS. Peripheral arterial disease, prevalence and cumulative risk factor profile analysis. *Eur J Prev Cardiol*. 2014;21(6):704-711.
24. Lu L, Mackay DF, Pell JP. Meta-analysis of the association between cigarette smoking and peripheral arterial disease. *Heart*. 2014;100(5):414-423.
25. Althouse AD, Abbott JD, Forker AD, Bertolet M, Barinas-Mitchell E, Thurston RC, Mulukutla S, Aboyans V, Brooks MM, BARI 2D Study Group. Risk factors for incident peripheral arterial disease in type 2 diabetes: results from the Bypass Angioplasty Revascularization Investigation in type 2 Diabetes (BARI 2D) Trial. *Diabetes care*. 2014;37(5):1346-1352.

26. Nehler MR, Duval S, Diao L, Annex BH, Hiatt WR, Rogers K, Zakharyan A, Hirsch AT. Epidemiology of peripheral arterial disease and critical limb ischemia in an insured national population. J Vasc Surg Cases. 2014;60(3):686-695.