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Original Research Article

Determinants of Doppler-confirmed lower-limb atherosclerosis in asymptomatic type 2 diabetes: cross-sectional evidence from a tertiary centre in South India

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ABSTRACT

Background: Peripheral artery disease (PAD) in type 2 diabetes is frequently asymptomatic yet clinically significant, has multifactorial risk factors, the identification of which enable appropriate preventive strategies. Aims of study were- to identify clinical and biochemical determinants of Doppler-confirmed lower-limb atherosclerosis (PAD) in asymptomatic adults with type 2 diabetes and to establish the in- hospital prevalence of PAD in the study population. It was an observational cross-sectional study conducted at a tertiary care centre in South India.
Methods: Adults ≥40 years with type 2 diabetes, asymptomatic for PAD were screened for PAD using colour duplex doppler, those with PAD were evaluated for demographic factors, diabetes duration, glycaemia (HbA1c), lipid profile, and diabetes complications [retinopathy, proteinuria/renal involvement, neuropathy, and coronary artery disease (CAD)]. Statistical analysis used was χ^2/Fisher's exact test for categorical variables and Welch's t-test for continuous variables. Analyses were performed in R, version 4.1.1
Results: Among 320 participants, PAD prevalence was 41.9% (n=134). PAD was associated with older age, longer diabetes duration, higher HbA1c, lower HDL and higher triglycerides, as well as retinopathy, proteinuria/renal involvement, neuropathy, and coronary artery disease (all $p<0.001$). Gender, LDL cholesterol and total cholesterol were not associated significantly with PAD ($p>0.05$).
Conclusions: Age, glycaemic burden, atherogenic dyslipidaemia, and microvascular/atherosclerotic comorbidities can help identify higher-risk subgroups for targeted PAD screening in asymptomatic type 2 diabetes.

Keywords: Coronary artery disease, Diabetic neuropathy, Diabetic retinopathy, Dyslipidaemias, HbA1c, Peripheral vascular diseases, Proteinuria, Risk factors

INTRODUCTION

Peripheral arterial disease (PAD) is the third most common clinical manifestation of atherosclerosis after coronary artery disease and stroke, with an estimated global prevalence exceeding 200 million people.[1,2] It contributes substantially to cardiovascular morbidity and mortality, with affected individuals experiencing a two- to six-fold increased risk of myocardial infarction, stroke and cardiovascular death.[3,4]

In diabetics, PAD remains underdiagnosed, despite its progression, partly due to its coexistence with peripheral neuropathy, which mask classical symptoms such as intermittent claudication. This results in a late detection once significant limb damage has occurred.[5-7]

Regional studies suggest that Indian patients often present younger, with clustering of multiple risk factors, compared with Western populations.[7]

Thus, in patients with type 2 diabetes mellitus, there is a need to identify risk factors that contribute to PAD, especially before its progression, so that these factors can be intervened upon to potentially reduce PAD incidence, severity and morbidity.

Objectives

Objective were to identify clinical and biochemical determinants of Doppler-confirmed lower-limb atherosclerosis (PAD) in asymptomatic adults with type 2 diabetes.

METHODS

Study design and setting

Observational, cross-sectional study conducted in the inpatient and outpatient settings of hospitals affiliated to Bangalore Medical College and Research Institute and Sri Jayadeva Institute of Cardiovascular Sciences and Research in Bengaluru, India from September 2021 to September 2024.

Participants

Inclusion criteria were adults aged ≥40 years with type 2 diabetes mellitus who provided written informed consent and were asymptomatic for PAD. Exclusion criteria included refusal of consent, inability to lie supine, intensive-care status, active respiratory illness, congestive heart failure, significant valvular disease, suspected arteritis or collagen vascular disease, hypercoagulable states, and current smokers.

Outcome and variables

The study patients were assessed for PAD. PAD was defined by colour duplex Doppler evidence of lower-limb arterial atherosclerosis. Candidate determinants including age, sex, duration of diabetes, HbA1c, fasting lipid profile (HDL, triglycerides, total cholesterol), and complications-retinopathy, proteinuria/renal involvement (present/absent), neuropathy, and coronary artery disease were noted.

Statistical analysis

Categorical variables were compared using Chi – square or Fisher's exact test; continuous variables were analysed using Welch's T-test. A two-sided α=0.05 denoted significance. Analyses were performed in R, version 4.1.1.

RESULTS

Demographics

A total of 320 participants were included; out of the 320 samples collected, 158 patients (49.38%) were male and 162 patients (50.63%) were female. 102 (31.87%) were of 50 years of age or lesser, 101 (31.56%) were aged between 51 and 60 years, 77 (24.06%) were between 61 to 70 years of age and 40 (12.5%) were greater than 70 years of age, mean age was 57.43 years. The median duration of T2DM was 7 years (IQR 3, 13). The mean LDL was 78.74 mg/dl (SD=27.97). The mean total cholesterol was 141.10 mg/dl (SD=33.73). Median serum triglyceride level was 122.5 mg/dl (IQR=90, 162). Mean HbA1c was 9% (SD=1.78).

Analysis data

PAD prevalence was found in 134 patients (41.9%) using lower limb arterial doppler ultrasound among whom 70 patients were male and 64 patients were female. The individuals with PAD were significantly older compared to those without PAD (p<0.001) and the prevalence of PAD increased as the age increased (≤50 years: 9.7%, 51-60 years: 32.1%, 61-70 years: 35.8%, >70 years: 22.4%) (Table 1). Median duration of diabetes was significantly higher in those with PAD (12 years versus 5 years, p<0.001) (Table 2). The mean glycated hemoglobin was significantly higher in the PAD group (9.6±1.7%) compared to those without it (8.6±1.7%), p<0.001 (Figure 1). Those with PAD had significantly lower HDL cholesterol levels ((26.0±8.1 mg/dl) versus (41.6±7.0 mg/dl), p<0.001) (Figure 2). Further, the PAD population also had significantly higher median serum triglyceride levels, p<0.001 (Table 3).

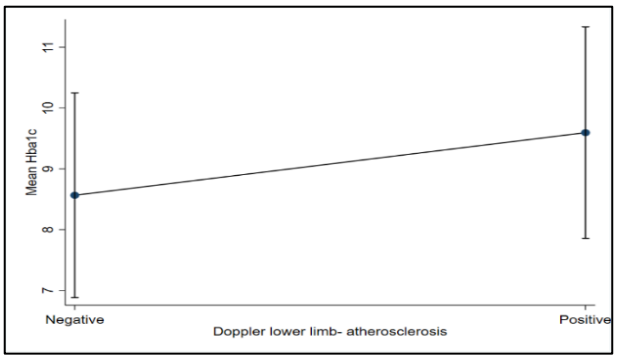

Figure 1: HbA1c and atherosclerosis.

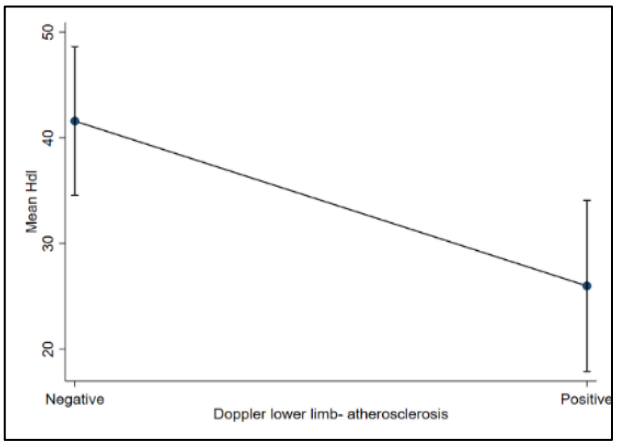

Figure 2: HDL cholesterol and atherosclerosis.

Peripheral arterial disease detected on Doppler was found to cluster significantly with other microvascular and macrovascular complications of diabetes. Among patients with diabetic retinopathy, 74% had PAD compared to only 24% of those without retinopathy (p<0.001) (Table 4). Similarly, PAD was present in 83% of patients with proteinuria versus 25% of those without proteinuria (p<0.001) (Table 5). A strong association was also observed with neuropathy, with 85% of neuropathy patients showing PAD compared to 32% in those without neuropathy (p<0.001) (Table 6). In terms of macrovascular complications, 87% of patients with coronary artery disease (CAD) had concomitant PAD, whereas only 26% of those without CAD had PAD (p<0.001) (Table 7). No significant differences observed in total cholesterol or LDL cholesterol levels between patients with and without Doppler-confirmed PAD; mean total cholesterol was 142.0±43.6 mg/dl in PAD patients versus 140.4±24.4 mg/dl in non-PAD patients (p=0.682), while mean LDL was 78.5±34.1 mg/dl in PAD patients compared to 78.9±22.7 mg/dl in those without PAD (p=0.885). Similarly, gender distribution was not significantly different, with PAD present in 44% of males and 40% of females (p=0.384).

Table 1: Age and pad risk.

Age (in years)	Doppler lower limb- atherosclerosis		Total (%)	P value
	Negative (%)	Positive (%)		
≤50	89 (87)	13 (13)	102 (100)	<0.001
51-60	58 (57)	43 (43)	101 (100)	
61-70	29 (38)	48 (62)	77 (100)	
>70	10 (25)	30 (75)	40 (100)	
Total	186 (58)	134 (42)	320 (100)	

Table 2: Duration of type 2 diabetes mellitus and PAD.

Doppler lower limb-atherosclerosis	N	Duration OD type II diabetes mellitus		P value
		Median	IQR	
Negative	186	5	(3, 10)	<0.001
Positive	134	12	(7, 16)	

Table 3: Triglycerides and atherosclerosis.

Doppler lower limb atherosclerosis	N	Triglycerides		P value
		Median	IQR	
Negative	186	108	(84, 141)	<0.001
Positive	134	156	(116, 192)	

Table 4: Eye complications and atherosclerosis.

Eye complication	Doppler lower limb-atherosclerosis		Total (%)	P value
	Negative (%)	Positive (%)		
Absent	156 (76)	50 (24)	206 (100)	<0.001
Present	30 (26)	84 (74)	114 (100)	
Total	186 (58)	134 (42)	320 (100)	

Table 5: Proteinuria and atherosclerosis.

Proteinuria	Doppler lower limb- atherosclerosis		Total (%)	P value
	Negative (%)	Positive (%)		
Present	16 (17)	76 (83)	92 (100)	<0.001
Absent	170 (75)	58 (25)	228 (100)	
Total	186 (58)	134 (42)	320 (100)	

Table 6: Neuropathy and atherosclerosis.

Neuropathy	Doppler lower limb- atherosclerosis		Total (%)	P value
	Negative (%)	Positive (%)		
Yes	9 (15)	52 (85)	61 (100)	<0.001
No	177 (68)	82 (32)	259 (100)	
Total	186 (58)	134 (42)	320 (100)	

Table 7: Coronary artery disease and atherosclerosis.

Coronary artery disease	Doppler lower limb- atherosclerosis		Total (%)	P value
	Negative (%)	Positive (%)		
Yes	11 (13)	73 (87)	84 (100)	<0.001
No	175 (74)	61 (26)	236 (100)	
Total	186 (58)	134 (42)	320 (100)	

DISCUSSION

Our study evaluated the determinants of PAD in an asymptomatic T2DM cohort where PAD was confirmed by Doppler. We included a detailed assessment of microvascular complications and concurrent cardiometabolic profiling in a single tertiary-care setting, thereby reducing spectrum bias and improving clinical relevance. In line with findings from other diabetes cohorts, our study demonstrated that PAD was more frequent with advancing age, longer duration of diabetes, higher HbA1c, lower HDL, and elevated triglycerides. Further, PAD also clustered with retinopathy, nephropathy/proteinuria, neuropathy, and coronary artery disease, reflecting potential common endothelial and atherothrombotic mechanisms.[4-6,11,12,15-21]

However, no significant association was found between gender (p=0.384), serum LDL cholesterol levels (p=0.885) and serum total cholesterol levels (p=0.682) with lower-limb atherosclerosis in our study. A possible explanation can be the remodelling of the lipid profile by insulin resistance. Elevated free fatty acids associated with insulin resistance stimulate hepatic VLDL overproduction, and these VLDL particles exchange triglycerides with both HDL and LDL. Triglyceride-enriched HDL is cleared more rapidly, reducing the pool available for reverse cholesterol transport. Triglyceride-enriched LDL is converted to smaller, denser particles that traverse the arterial wall more easily and oxidize readily-features that make them highly atherogenic. As a result, LDL-cholesterol concentration may show little association with atherosclerosis in T2DM, because risk is driven by the small, dense LDL phenotype rather than by LDL-C quantity per se. Likewise, since total cholesterol incorporates both LDL-C and HDL-C, the fall in HDL that accompanies insulin resistance can lower total cholesterol even while cardiovascular risk rises, helping to explain the non-significant link between total cholesterol and lower-limb atherosclerosis in this study.[7-10,12]

Clinically, recognising this diabetic dyslipidaemia pattern is important because PAD portends elevated cardiovascular risk even when LDL-C appears "acceptable"; Ankle brachial index adds incremental prognostic information to risk scores and supports the need for comprehensive risk-factor modification.[14,15] In addition, structured walking and physical-activity interventions improve functional status and cardiovascular outcomes in PAD, reinforcing the case for early identification and secondary prevention in this high-risk group.[13] Consistent with Indian cohort data, our patients tended to present at a relatively younger age with clustering of multiple risk factors, and local series similarly report high diabetes burden and frequent symptomatic presentations.[17-21] These show that PAD is part of a broader systemic disorder, emphasizing the importance of addressing overall cardiometabolic risk factors along with limb-specific therapy.[20-21]

Finally, the strong associations we observed between PAD and coexisting micro- and macrovascular complications (retinopathy, proteinuria/renal involvement, neuropathy, and CAD) emphasise that PAD is a marker of widespread vasculopathy in T2DM; anticipation, screening and timely management of these complications are therefore warranted in patients with PAD to reduce morbidity and mortality.[10,12,15,16]

Limitations

This study has certain limitations. The relatively small sample size and single-city, tertiary-care setting may limit the external validity of the findings. In addition, the cross-sectional design restricts the ability to draw causal inferences. Long-term outcomes were not assessed, and advanced imaging modalities such as CTA or MRA were not available for all patients, which may have constrained the depth of vascular assessment.

CONCLUSION

Older age, poor glycaemic control, abnormal lipid patterns, and the presence of microvascular or atherosclerotic complications can help identify high-risk subgroups of asymptomatic adults with type 2 diabetes who would benefit from targeted PAD screening and preventive measures. Further, comprehensive risk factor management, beyond LDL-C alone, is essential for improving outcomes.

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