Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Research

Assessment of Peripheral Arterial Disease among Type 2 Diabetes Patients in Calabar, Nigeria

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Abstract

Background: Peripheral Arterial Disease (PAD) is a significant complication among patients with Type 2 Diabetes Mellitus (T2DM), characterized by atherosclerosis that leads to reduced blood flow to the extremities. This article assesses the traditional risk factors for PAD and the predictive value of the new inflammatory biomarkers like fibrinogen and C-reactive protein (CRP), and the implications of PAD in T2DM patients, drawing from recent studies and findings. The presence of PAD in T2DM patients poses serious health risks, including increased risk of foot ulcers, limb amputation, and cardiovascular events, necessitating comprehensive cardiovascular risk management. The study aims to assess the effectiveness of various diagnostic tests for PAD, particularly the Ankle-Brachial Index (ABI), in detecting PAD and stratifying cardiovascular risk in T2DM patients.

Methodology: The study population comprises the recruitment of 112 Type 2 DM patients and an equal number and sex matched healthy participants as controls from three centres in Calabar, making a total of 224 participants. Socio-demographic information was collected. After physical examination and anthropometric measurements, the ABI was performed using a Doppler ultrasound device. Descriptive statistics were used to summarize clinical and demographic characteristics, and comparative analysis was done using chi-square for categorical variables and t-test for continuous variables. Logistic regression was used for independent risk factors associated with PAD.

Results: The median ages for the Type 2 DM patients and the controls were 58 years (IQR 10) and 58 years (IQR 11), respectively. The prevalence of PAD using ABI<0.9 in this study was 37.5% in people living with type 2 diabetes and 14.3% in controls. The prevalence of PAD for Type 2 DM patients and controls using symptoms of palpation of pedal pulsations and intermittent claudication was 17.0% vs 3.6% and 11.6% vs 2.7% respectively. There was a statistically significant relationship between advanced age, hypertension, duration of diabetes, glycaemic control, fibrinogen, as well as CRP, and PAD among people living with Type 2 diabetes. After multiple regression analysis, the predictors of PAD in this study were age, duration of Diabetes, and elevated serum CRP. There was no correlation between smoking, obesity, and lipid profiles with PAD.

Conclusion: There is a high prevalence of peripheral artery disease among people with T2DM in Calabar. The use of ABI is of great value in the detection of PAD, as evidenced by a more objective assessment of PAD compared to intermittent claudication and reduced/absent pedal pulses. Routine screening of PLWDM for PAD using ABI would enhance early diagnosis and intervention.

Keywords: Peripheral Arterial Disease; Type 2 Diabetes; Ankle Brachial Index; Doppler Ultrasound.

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How to Cite: Enang OE, Araga AN, Okpa HO, Essien OE. Assessment of Peripheral Arterial Disease among Type 2 Diabetes Patients in Calabar, Nigeria. Niger Med J 2025;66 (4):1315-1332.https://doi.org/10.71480/nmj.v66i4.560.

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Introduction

Peripheral arterial disease (PAD) is a chronic complication of diabetes mellitus and is a risk factor for foot ulceration and amputation. It is more common in patients with diabetes compared to those without diabetes, with the occurrence being up to four times higher in diabetic patients [1]. PAD significantly reduces the quality of life, which worsens with disease progression[2]. Additionally, it is associated with an increased risk of cardiovascular complications such as stroke and myocardial infarction [2, 3]. Symptoms like intermittent claudication, and calf pain at rest can indicate PAD, but in patients with diabetes, these symptoms may be masked by the presence of peripheral neuropathy [1].

Peripheral artery disease (PAD) is the result of atherosclerosis in the arteries of the lower extremities and is often associated with atherothrombosis in other parts of the body [1]. The ankle-brachial index (ABI) is commonly used to diagnose PAD non-invasively [4, 5]. However, in people with diabetes mellitus, ABI may not be a reliable indicator of PAD due to arterial stiffening caused by calcification of the tunica media [6]. It's important to note that atherosclerotic disease in diabetic patients is often unevenly distributed, and the extremities' distal vessels are commonly affected [7]. This can lead to inaccurate ABI measurements in diabetic patients [6,7]. Despite these limitations, ABI can still be used to determine the prognosis of PAD in affected limbs and to predict the risk of acute myocardial infarction [4]. ABI is calculated as the ratio of the highest ankle systolic blood pressure (SBP) to the highest brachial SBP. An ABI of less than 0.90 is used to diagnose PAD. The sensitivity of ABI for PAD diagnosis has been reported to range from 38% to 90%, while an ABI of less than 0.90 has a specificity approaching 100% when compared to angiography [5, 8].

There are various factors linked to the risk of PAD, which can be categorized into traditional and novel risk factors. Traditional risk factors, commonly observed in other atherosclerotic vascular diseases, include hypertension, dyslipidemia, diabetes, age, and smoking [9,10]. Novel risk factors are said to comprise hyperhomocysteinemia, along with inflammatory markers such as CRP, fibrinogen, and leukocytosis [10, 11].

Materials and Methods:

This was a multicentre comparative cross-sectional study. Two Hundred and Twenty-Four (224) subjects were recruited into the study (112 T2DM patients and an equal number of age and sex-matched, apparently healthy adults served as controls). A proportionate stratified sampling technique was used to determine the number of diabetes patients that were recruited from each of the three centres (UCTH, NNRH, and GHC). A systematic random sampling technique was then used for patient selection. History was taken; clinical examination, anthropometry was also performed, and ankle brachial index was measured using an 8MHz LifeDop Summit handheld Doppler device. PAD was defined as AB1 < 0.9 in at least one limb. Venous blood was collected to measure serum total cholesterol, HDL, triglycerides, HbA1c, hs-CRP, and fibrinogen. The data for each participant were collected from the complete questionnaire, as well as from anthropometric measurements, physical examination findings, ankle-brachial index (ABI), and results of laboratory investigations. This information was then entered into Microsoft Excel and stored in an encrypted format with a password. We used Statistical Package for Social Sciences (SPSS) version 26.0 for data analysis. To compare results between control and T2DM patients, we used Student's t-test to compare the ankle-brachial index and results of biochemical assays. We also conducted a test of normality to check whether the data were normally distributed. Furthermore, we assessed the correlation between peripheral arterial disease (PAD) and biochemical parameters (FLP, HBA1C, hs-CRP, and fibrinogen) using Pearson's correlation coefficient (r). We set the significance level at 5% ($p<0.05$). Variables that showed statistical significance during bivariate analysis were further analyzed with logistic regression (multivariate analysis) at a 5% significance level and 95% confidence interval.

The study received ethical approval from the Health Research Ethics Committee of the University of Calabar Teaching Hospital. Written informed consent was obtained from all participants before collecting their data. The study process, benefits, and possible risks were thoroughly explained to the participants, and they were assured of confidentiality and safety. Participants had the freedom to withdraw from the study at any time without facing any consequences. Those who declined consent were excluded from the study but were not denied quality care.

Results

The median ages for the Type 2 DM patients and the controls were 58 years (IQR 10) and 58 years (IQR 11), respectively. The prevalence of PAD using ABI<0.9 in this study was 37.5% in people living with type 2 diabetes and 14.3% in controls. The prevalence of PAD for Type 2 DM patients and controls using symptoms of palpation of pedal pulsations and intermittent claudication was 17.0% vs 3.6% and 11.6% vs 2.7% respectively. There was a statistically significant relationship between advanced age, hypertension, duration of diabetes, glycaemic control, fibrinogen, as well as CRP, and PAD among people living with Type 2 diabetes. After multiple regression analysis, the predictors of PAD in this study were age, duration of Diabetes, and elevated serum CRP. There was no correlation between smoking, obesity, and lipid profiles with PAD

In this study, 112 Type 2 DM patients receiving care at UCTH, NNRH, and GHC, as well as 112 age and sex-matched controls (apparently healthy adults), were included. The median ages for the Type 2 DM patients and the controls were 58 years (IQR 10) and 58 years (IQR 11), respectively. As shown in Table 1, the distribution of the respondents' marital status, occupation, educational status, and smoking habits differed significantly between the two groups. There was a higher proportion of widows/widowers and singles in the Type 2 DM group compared to the control group (17.0% and 6.3% versus 8.9% and 0.9% respectively). Additionally, all the retirees and past smokers were in the Type 2 DM group, with none in the control group (7.1% and 10.7% versus 0.0% and 0.0% respectively). Conversely, more respondents in the control group had completed secondary and post-secondary education compared to those in the diabetic group (25.9% and 66.1% versus 16.1% and 58.0% respectively). Furthermore, the median income was higher in the control group compared to the diabetic group (N71,000, IQR 71,250 versus N100,000, IQR 106,500). However, the distributions of the respondents' age group, sex, tribe, and religion were not significantly different between the two groups.

Table 1: Socio-demographic characteristics of Type 2 DM patients and their controls

Variables	Type 2 DM	Controls	X^2	p-value
	Freq. (%)	Freq. (%)		
Age group (yrs)				
40 – 49	8 (7.1)	8 (7.1)	0.05	0.993
50 – 59	53 (47.3)	53 (47.3)		
60 – 69	38 (33.9)	39 (34.8)		
≥ 70	13 (11.6)	12 (10.7)		
Sex				
Male	30 (26.8)	30 (26.8)	0.00	1.000
Female	82 (73.2)	82 (73.2)		
Ethnicity				
Efik	30 (26.8)	32 (28.6)	5.55	0.235
Ibibio	20 (17.9)	19 (17.0)		

Ejagham	23 (20.5)	13 (11.6)		
Igbo	8 (7.1)	16 (14.3)		
Others	31 (27.7)	32 (28.6)		
Religion				
Christianity	106 (94.6)	110 (98.2)	FET	0.280
Islam	6 (5.4)	2 (1.8)		
Marital Status				
Single	7 (6.3)	1 (0.9)	FET	0.012*
Married	86 (76.8)	99 (88.4)		
Widow/Widower	19 (17.0)	10 (8.9)		
Separated/Divorced	0 (0.0)	2 (1.8)		
Occupation				
Actively employed	104 (92.9)	112 (100.0)	FET	0.007*
Retiree	8 (7.1)	0 (0.0)		
Education				
No formal	12 (10.7)	1 (0.9)	15.70	0.001*
Primary	17 (15.2)	8 (7.1)		
Secondary	18 (16.1)	29 (25.9)		
Post-secondary	65 (58.0)	74 (66.1)		
Smoking				
Never smoked	100 (89.3)	112 (100.0)	12.68	<0.001*
Past smoker	12 (10.7)	0 (0.0)		

***Significant p-value, FET- Fisher's Exact Test**

The comparison of anthropometric measures and biochemical parameters between the diabetic group and their controls (see Table 2) showed that the diabetic patients were significantly more overweight, with higher average waist and hip circumferences. Additionally, the average waist-hip ratio and all the biochemical parameters were significantly higher among the diabetic patients in comparison to their controls.

Table 2: Comparison of anthropometric measures and biochemical parameters of Type 2 DM patients and controls in Calabar

Variables	Group	Mean	SD	t	p-value
BMI (kg/m^2)	Type 2 DM	29.52	6.96	3.16	<0.001*
	Control	26.35	2.64		
WC (cm)	Type 2 DM	99.19	14.34	5.64	<0.001*
	Control	89.64	10.74		
HC (cm)	Type 2 DM	106.29	12.66	2.14	0.034*
	Control	102.50	13.91		
WHR	Type 2 DM	0.93	0.09	4.69	<0.001*
	Control	0.88	0.05		

TOTAL FLP	Type 2 DM	6.18	2.88	4.18	<0.001*
	Control	4.98	0.98		
HDL	Type 2 DM	1.53	0.68	2.01	0.046
	Control	1.37	0.51		
LDL	Type 2 DM	3.76	2.55	4.04	<0.001*
	Control	2.73	0.85		
TG	Type 2 DM	1.96	1.21	0.24	0.808
	Control	1.93	0.59		
HbA1c	Type 2 DM	7.98	6.88	5.34	<0.001*
	Control	4.47	1.10		
C-reactive protein	Type 2 DM	9.67	6.10	6.12	<0.001*
	Control	5.05	5.16		
Fibrinogen	Type 2 DM	393.57	120.28	9.62	<0.001*
	Control	274.50	51.77		

***Significant p-value, SD – Standard Deviation**

The prevalence of peripheral artery disease (PAD) was compared between Type 2 diabetes mellitus (DM) patients and their age and sex-matched controls. The results are summarized in the tables below:

The prevalence of PAD in Type 2 DM patients, as assessed by the presence of intermittent claudication, was significantly higher compared to the controls (17.0% versus 3.6%, $p = 0.001$).

PAD prevalence, assessed using palpation of pedal pulses (reduced/absent posterior tibial artery and dorsalis pedis pulses), was significantly higher in Type 2 DM patients compared to controls (11.6% versus 2.7%, $p < 0.009$).

Isolated reduced/absent pulsation of the posterior tibial and dorsalis pedis arteries was also compared. The results showed that Type 2 DM patients had a significantly higher prevalence compared to controls (20.5% versus 3.6%, $p < 0.001$ for posterior tibial artery pulsation; 14.3% versus 4.5%, $p = 0.012$ for dorsalis pedis artery pulsation).

The prevalence of PAD, as assessed using ankle-brachial index (ABI), was significantly higher among Type 2 DM patients compared to controls (37.5% versus 8%, $p < 0.001$).

Additionally, among the 112 Types 2 DM patients, the distribution of PAD severity was as follows: 2 (1.8%) had severe PAD, 12 (10.7%) had moderate PAD, 28 (25.0%) had mild PAD, 2 (1.8%) had hypercalcified vessels, and 68 (60.7%) had normal ABI. Figure 1 provides a visual representation of these findings.

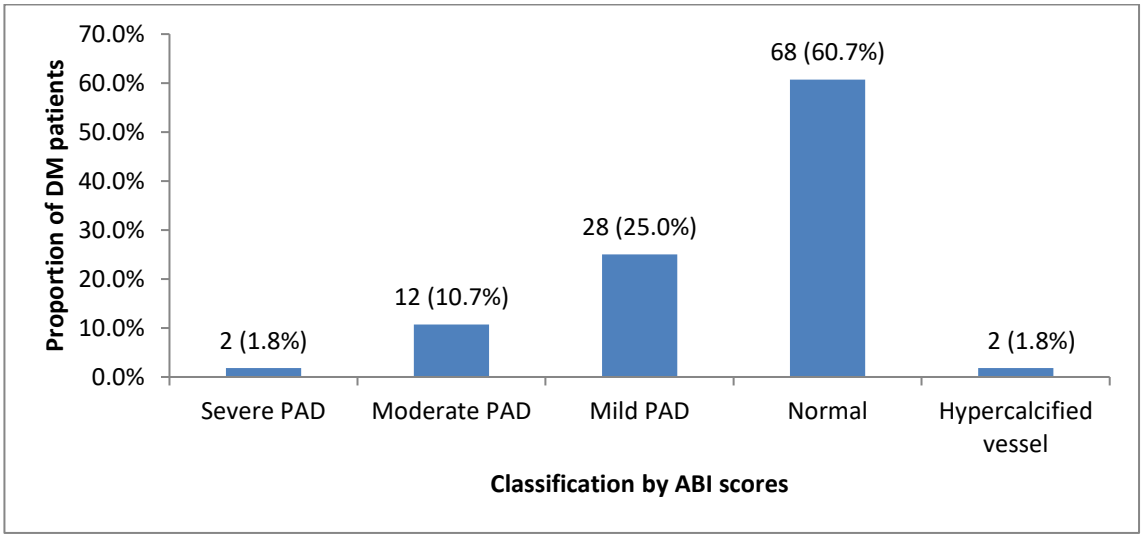

Figure 1: Frequency distribution of PAD severity among Type 2 DM patients (n = 42)

Table 3: Prevalence of Peripheral Artery Disease as measured by intermittent claudication among patients with diabetes and controls

Peripheral Artery Disease	Type 2 DM (n = 112)		Control (n = 112)		X^2	p-value
	Frequency	(%)	Frequency	%		
Present	19	17.0	4	3.6	10.90	< 0.001*
Absent	93	83.0	108	96.4		

***Significant p-value**

Table 4: Prevalence of Peripheral Artery Disease as measured by reduced/absent palpation of both posterior tibial and dorsalis pedis artery among patients with Type 2 DM and controls.

PAD by palpation	Type 2 DM (n = 112)		Control (n = 112)		X^2	p – value
	Frequency	(%)	Frequency	%		
Present	13	11.6	3	2.7	6.73	0.009*
Absent	99	88.4	109	97.3		

***Significant p-value**

Table 5a: Isolated absence/reduced palpation of posterior tibial arteries among patients with Type 2 DM and controls

PAD by palpation	Type 2 DM (n = 112)		Control (n = 112)		X^2	p-value
	Frequency	(%)	Frequency	%		
Posterior tibia						
Present	23	20.5	4	3.6	15.2o	0.001*
Absent	89	79.5	108	96.4		

Table 6: Prevalence of Peripheral Artery Disease as measured by ABI among patients with Type 2 DM and controls in Calabar

Peripheral Artery Disease	Type 2 DM (n = 112)		Control (n = 112)		X^2	p-value
	Frequency	(%)	Frequency	%		
Present	42	37.5	9	8.0	27.65	< 0.001*
Absent	70	62.5	103	92.0		

***Significant p-value**

The study explored the connection between traditional risk factors of peripheral artery disease (PAD), such as smoking, dyslipidemia, hypertension, age, glycemic control, and body mass index (BMI) in patients with Type 2 diabetes. The Chi-square test of independence was used for this exploration. Table 7 illustrates that there was no significant correlation between smoking history, obesity (BMI), fasting serum triglyceride, total cholesterol, HDL, and LDL levels, and the occurrence of peripheral artery disease. However, there were significant associations between age, hypertension, and HbA1C level of the Type 2 diabetic patients and the occurrence of PAD. The percentage of PAD patients was significantly higher among those who were 70 years and older compared to younger individuals ($p = 0.003$), those with hypertension compared to those without (43.4% versus 20.7%, $p = 0.030$), and those with abnormal HbA1C levels compared to those with normal HbA1C levels (51.6% versus 18.2%, $p < 0.001$). There was no significant difference in the mean waist circumference of diabetic patients with PAD compared to those without PAD (98.67 ± 14.75 years versus 99.50 ± 14.18 years, $p = 0.767$), as shown in Table 8. Furthermore, as indicated in Table 9, the mean duration of diabetes was higher among those with PAD compared to those without PAD (12.24 ± 7.88 years versus 6.66 ± 5.24 years, $p < 0.001$). Figure 2 shows that most diabetic patients have had the disease for either 1–10 years (62.5%) or 11–20 years (33.0%), with only a few of them (4.5%) having had the disease for more than 20 years.

Table 7: Relationship between traditional risk factors and PAD among Type 2 DM patients in Calabar

Variables	Peripheral Artery Disease		X^2	p-value
	Present (%)	Absent (%)		
Age group (yrs)				
40 – 49	3 (37.5)	5 (62.5)	FET	0.003*
50 – 59	16 (30.2)	37 (69.8)		
60 – 69	12 (31.6)	26 (68.4)		
≥ 70	11 (84.6)	2 (16.4)		
Sex				
Male	11 (36.7)	19 (63.3)	0.01	0.912
Female	31 (37.8)	51 (62.2)		
Smoking				
Never Smoked	38 (38.0)	62 (62.0)	FET	1.000
Past Smoker	4 (33.3)	8 (66.7)		
Hypertension				

Yes	36 (43.4)	47 (56.6)	4.72	0.030*
No	6 (20.7)	23 (79.3)		
Triglyceride				
Normal	23 (40.4)	34 (59.6)	0.40	0.526
Abnormal	19 (34.5)	36 (65.5)		
Total Cholesterol				
Normal	17 (38.6)	27 (61.4)	0.04	0.842
Abnormal	25 (36.8)	43 (63.2)		
HDL				
Normal	29 (37.2)	49 (62.8)	0.01	0.915
Abnormal	13 (38.2)	21 (61.8)		
LDL				
Normal	16 (42.1)	22 (57.9)	0.52	0.471
Abnormal	26 (35.1)	48 (54.9)		
HbA1C				
Normal	10 (18.2)	45 (81.8)	17.21	< 0.001*
Abnormal	32 (56.1)	25 (43.9)		
Obesity (BMI)				
Yes	15 (31.3)	33 (68.7)	1.40	0.237
No	27 (42.2)	37 (67.8)		

*Significant p-value, FET- Fisher's Exact Test

Table 8: Comparison of mean waist circumference by PAD status among Type 2 DM patients in Calabar

Waist Circumference	Group	Mean	SD	T	p-value
	PAD	98.67	14.75	-0.30	0.767
	No PAD	99.50	14.18		

SD – Standard Deviation, *Significant p-value

Table 9: Comparison of duration of diabetes by PAD status among Type 2 DM patients in UCTH, Calabar

Duration of DM	Group	Mean	SD	t	p-value
	PAD	**12.24**	**7.88**	**4.50**	**< 0.001***
	No PAD	**6.66**	**5.24**		

SD – Standard Deviation, *Significant p-value

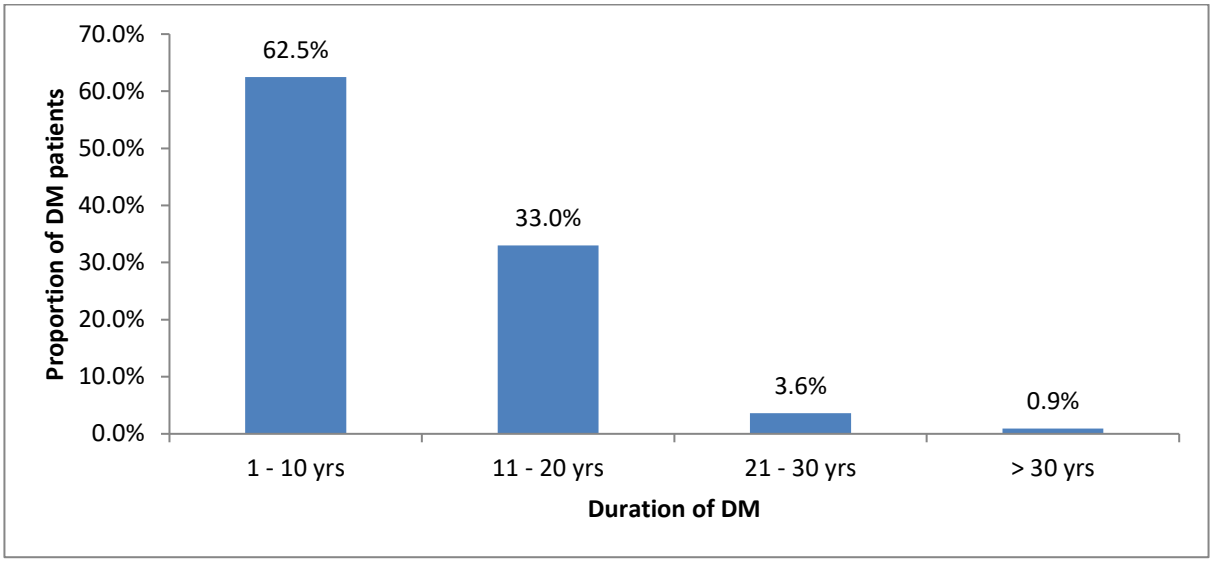

Figure 2: Frequency distribution of duration of disease among Type 2 DM patients in Calabar

In this study, we examined the connection between peripheral artery disease (PAD) as assessed by ABI (ankle-brachial index) and inflammatory markers (C-reactive protein and fibrinogen levels) in patients with Type 2 diabetes. We used Pearson's correlation coefficient for our analysis, and the results are presented in Figure 3. Our findings revealed significant negative associations between PAD (measured by ABI) and fibrinogen levels ($r = -0.83$, $p < 0.001$), as well as between ABI values and C-reactive protein levels ($r = -0.35$, $p < 0.001$). Essentially, lower ABI values, indicating greater severity of PAD, were linked to higher levels of C-reactive protein and serum fibrinogen levels.

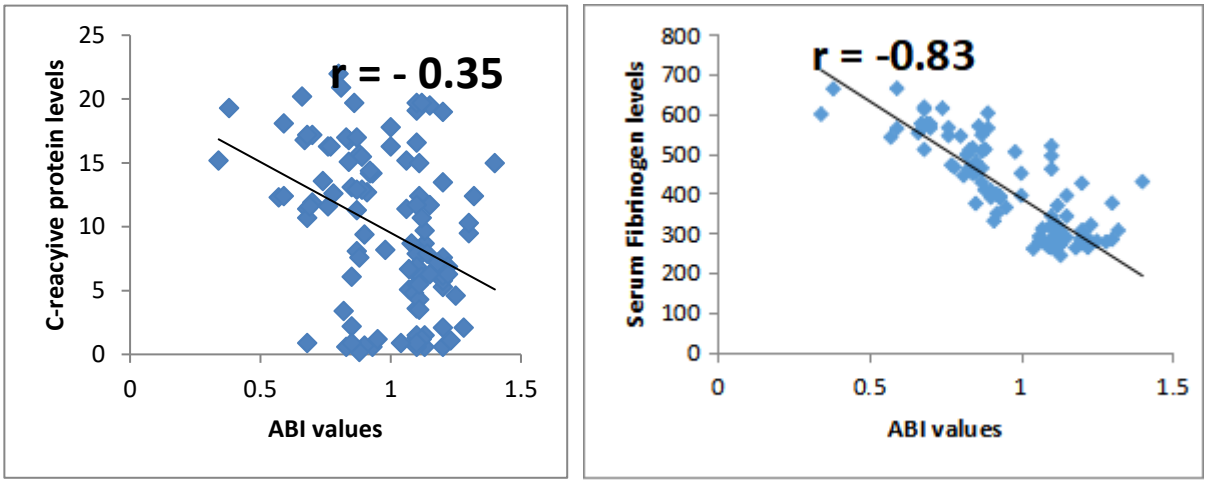

Figure 3: Relationship between ABI and inflammatory markers in Type 2 DM patients

A hierarchical multiple regression analysis was conducted to assess the ability of serum C-reactive protein and fibrinogen levels in predicting PAD based on ABI levels, while controlling for age, duration of Type 2 DM, and HbA1C levels, as presented in Table 10. The results indicated that after controlling for age, duration of Type 2 DM, and HbA1C, only the C-reactive protein level was a significant predictor of PAD as measured by ABI values (beta = -0.01, p = 0.001).

Table 9: Multiple regression analysis of predictors of PAD among Type 2 DM patients

Predictors	Estimate	SE	p-value
Intercept	1.41	0.13	< 0.001*
Age	- 0.004	0.002	0.064*
Type 2 DM duration	- 0.006	0.003	0.034*
HbA1C	< 0.001	0.003	0.870
C-reactive protein	- 0.010	0.003	0.001*
Fibrinogen	< 0.001	< 0.001	0.438

SE – Standard Error of estimate

Discussion

Peripheral artery disease is common among people living with diabetes [12,13] and often occurs alongside vascular disease in other parts of the body[14,15]. Nearly 50% of patients with PAD do not show any symptoms [16]. The absence of symptoms in diabetic patients with peripheral artery disease is likely due to the co-existence of diabetic neuropathy, which impairs their ability to perceive pain [17]. PAD is a risk factor for foot ulceration and amputation [4,17] and is linked to a significantly increased risk of cardiovascular morbidity and mortality [18,19].

This study aimed to determine the prevalence of peripheral arterial disease using the ankle brachial index, as well as the correlation between traditional and non-traditional inflammatory risk factors and peripheral arterial disease in people living with diabetes mellitus in Calabar.

A total of 112 Type 2 diabetes mellitus (T2DM) patients receiving care in UCTH, NNRH, and GHC, and 112 age- and sex-matched controls (apparently healthy adults), were recruited for this study. The median ages for the T2DM patients and the controls were 58 years (IQR 10) and 58 years (IQR 11), respectively. The nearly identical ages observed in this study resulted from the use of age-matched controls. The mean age is similar to that reported by Soyoye et al in Southwest Nigeria, where they had mean ages of 56.12 ± 7.65 and 55.76 ± 7.49 years for T2DM and control participants, respectively [17]. Similarly, Obi et al, in their study of prevalence and predictors of lower extremity peripheral artery disease among adults with T2DM attending a tertiary hospital in Owerri, Nigeria, reported mean ages of 59.8 ± 10.7 and 59.6 ± 12.3 years for T2DM and control participants, respectively [20]. Out of the people living with diabetes mellitus, 30 (26.8%) were males, and 82 (73.2%) were females, while in the control group, 30 (26.8%) were males, and 82 (73.2%) were females, resulting in a near equal male-female ratio. The female-to-male ratio in this study was 1:2.8. Our diabetes clinic showed a higher proportion of females compared to males, consistent with a similar observation made by Soyoye et al [17] in a study in southwestern Nigeria. Yakubu et al [4] suggested that this trend could be attributed to females having a greater tendency to seek healthcare compared to males. The majority of participants in both the PLWDM (94.6%) and control group (98.2%) practice Christianity, which may be linked to the study being conducted in a Christian-populated region of South-South Nigeria.

There were significant differences in the occupational and educational levels between the two groups. The control group primarily consisted of hospital staff, resulting in a higher number of participants with secondary and post-secondary education levels, and all participants in the control group were employed. Additionally, there was a notable discrepancy in the history of smoking between the PLWDM and control groups, as individuals with a history of smoking were excluded from the control group:

The prevalence of Peripheral Artery Disease (PAD) varies depending on the method used for diagnosis. Studies have used different criteria, such as symptoms, absence of peripheral pulses, and Ankle-Brachial Index (ABI), to assess PAD. The prevalence of PAD was found to be higher among People Living with Diabetes (PLWD) compared to controls when using history of intermittent claudication and palpation, with percentages ranging from 11.6% to 17.0%. Using ABI<0.9, the prevalence of PAD was notably higher among PLWD (37.5%) compared to controls (8.0%). Studies across different regions in Nigeria, Cameroon, Ghana, Ethiopia, and Uganda reported varying prevalence of PAD, with PLWD showing higher prevalence [21-24].

Out of 112 Type 2 DM patients, 60.7% had normal ABI, 25.0% had mild PAD, 10.7% had moderate PAD, 1.8% had a severe form of PAD, and 1.8% had poorly compressed vessels. These findings were like reports from other studies [25,26].

The study found a significant association between increasing age and peripheral artery disease (PAD). This finding is consistent with several other studies [27,28, 29]. PAD was found to be more common among individuals with type 2 diabetes mellitus (T2DM) who are over 70 years old [9,30]. However, there was no statistically significant correlation between gender and PAD in this study. This is similar to reports by Yakubu et al [4], Mwebaze et al [25]. By contrast, Akpan et al [31] reported a higher prevalence of PAD among females. The higher prevalence among women could be due to a combination of hormonal differences between males and females and a higher risk of cardiovascular risk factors, such as a sedentary lifestyle, high-fat diet, and higher lipid levels [31]. Although other studies have reported different findings [4,17]. Additionally, the study did not find a correlation between smoking and PAD, which differs from other research that has identified smoking as a common risk factor for PAD [9,32,33]. A similar finding was reported by Rabia et al [34]. The smaller number of participants who smoked in the past and the minimal smoking dose in those who smoked may account for the absence of an association between smoking and PAD in this study.

The study found that hypertension was associated with peripheral artery disease (PAD), consistent with previous research [35,36, 37,38]. Hypertension has been known to affect vascular endothelial cell morphology, structure, and function, and vascular wall permeability. This contributes to the accumulation of fat and cells[44], leading to atherosclerosis and PAD[39]. Similarly, Yusuf et al [40] reported a significant association between hypertension and PAD [41,42]. However, dyslipidemia did not show a significant link to PAD in this study, possibly because most patients were taking statins. Similar results were reported by Yakubu et al [4], Mwebaze et al [15], Sartore et al [43], and Guan et al [44]. Obesity is an important cardiovascular risk factor and has been reported to be associated with PAD [45], and although obesity was more common among people living with diabetes (PLWD), there was no significant association between obesity and PAD. This is similar to a report by Oyelade et al [46]. Dissimilarly, there are reports from other studies in Nigeria that have shown a significant association between PAD and generalized obesity. On the other hand, poor glycemic control, as indicated by HbA1C levels of 7% or higher, showed a significant association with PAD. This is like findings reported by Soyoye et al [17], Umuerri et al [28] and Anumah et al [47], who reported a significant association between poor glycaemic control and PAD. Additionally, the duration of diabetes was found to be longer in those with PAD compared to those without PAD. These findings are in line with previous studies [47, 48 49] and highlight

the importance of managing hypertension, dyslipidemia, obesity, and glycemic control in preventing PAD.

The study found a significant relationship between elevated hs-CRP and PAD, which is consistent with similar reports from other studies in Nigeria [17], Ghana [50], and the Netherlands [51]. However, a study in Italy [52] did not find a significant relationship, possibly due to differences in sample size and the age of patients. Inflammation has been recognized as a risk marker and potentially a risk factor for atherosclerotic diseases, including PAD. Elevated CRP levels are strongly linked to the development of PAD [51]. Mechanisms of vascular damage due to CRP include down-regulation of endothelial nitric oxide synthase, increased expression of cell adhesion molecules, upregulation of LDL phagocytosis by macrophages, vascular-smooth muscle cell proliferation, and neo-intimal formation [53,54].

The study also showed a positive correlation between serum fibrinogen and peripheral artery disease, which is consistent with reports from other studies [55, 56, 57]. Fibrinogen is a cofactor in platelet activation and may directly contribute to plaque formation [55,58]. It is increased in diabetic patients, particularly in those with poor glycemic control, since glycosylated fibrinogen is less susceptible to plasmin degradation [55]. Together with hs-CRP, fibrinogen has been associated with a 1.5 – 2.5 increased risk for fatal events in type 2 DM patients [56]. Elevation of fibrinogen levels largely reflects the severity of the underlying LEAD [59].

Predictors of Peripheral Artery Disease in this study included increasing age, hypertension, duration of DM, poor glycemic control, fibrinogen, and hs-CRP. However, multivariate logistic regression analysis showed that only advancing age, duration of DM, and CRP were the predictors of PAD in T2DM participants. Similarly, other studies have reported advancing age and duration of diabetes as predictors of PAD [47, 60, 61]. Advanced age is associated with arterial stiffness and sclerosis, while diabetes is linked to an increased risk of cardiovascular diseases, with the severity of chronic glycemia associated with an increasing frequency of clinical events in all vascular beds. Additionally, CRP has been reported as a predictor of PAD. However, one study reported poor glycemic control as a predictor of PAD [47], which could be due to the larger sample size used in their study. HbA1c is a snapshot of a patient's glycemic status over three months and may not be a true reflection of their glycemic control over a longer period. Another study reported serum fibrinogen as a predictor of PAD [62], potentially explained by the longitudinal study design used for their research.

Conclusion:

The study found that peripheral artery disease (PAD) prevalence is high in people with type 2 diabetes (T2DM) at 37.5%, compared to 14.3% in age and sex-matched controls. The prevalence of PAD in this study, as measured by ankle-brachial index (ABI), was higher than when measured through a history of intermittent claudication (17.0% versus 3.6%) and palpation of the posterior tibial and dorsalis pedis arteries (20.5% versus 3.6% and 14.3% versus 4.5%). The study also revealed an association between peripheral arterial disease and traditional cardiovascular risk factors such as advancing age, hypertension, and duration of diabetes. Additionally, non-traditional risk factors like fibrinogen and C-reactive protein were found to be significantly higher in people with T2DM and peripheral arterial disease compared to those without it. Furthermore, advancing age and elevated hs-CRP levels were identified as predictors of PAD in T2DM patients.

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