***Original Research Article***

**Peripheral Arterial Disease in People Living With Type 2 Diabetes Mellitus**

**ABSTRACT**

**Background**

Diabetes mellitus (DM) is characterized by chronic hyperglycaemia due to absolute or relative deficiency of insulin affecting carbohydrate, fats and protein metabolism. It results in chronic vascular complications including macrovascular complications such as peripheral arterial disease (PAD), coronary artery disease and stroke. PAD results from narrowing of blood vessels with reduction in blood flow to the arms and legs (mostly). This results in ischaemic changes in the lower limbs and may ultimately cause ischaemic foot ulcers. PAD is a common macrovascular complication of type 2 DM and is usually asymptomatic. Palpation of peripheral pulses may not correlate with the degree of PAD. The ankle-brachial index (ABI) assessment using a handheld doppler is an objective and sensitive method of diagnosing PAD in people with type 2 diabetes mellitus (PLWDM). The aim of this study was to determine the prevalence of PAD and relationship between hypertension, dyslipidaemia and smoking in PLWDM.

**Methods**

Venous blood samples were collected for fasting plasma glucose, glycated haemoglobin (HbA1/c) and fasting lipid profile. PAD was obtained by determining the ABI using a handheld doppler. Data analysis was done using SPSS version 28.

**Results**

There was a total of 226 participants (126 cases, 100 controls). Mean age of cases was 52.4 years. The mean BMI for cases was 27.6kg/m2. Mean HbA1c of cases was 7.6± 1.5%. HDL in the controls was significantly higher than in the cases, p=0.0002, (<0.05). The prevalence of hypertension among cases with PAD was significantly higher (52.9% vs 7.6% in cases without PAD (*p*=0.0001). Prevalence of PAD was 27% with the ABI range of 0.62 – 0.89. Cases with hypertension had a significantly lower ABI (0.87 for both feet) than normotensive cases (0.94 for both feet), p=0.0001. Most of the diabetic smokers (71.4%) had PAD. About 76.5% of PLWDM who had PAD were asymptomatic. PAD was diagnosed in only 5 of the 18 subjects who had non-palpable foot pulses.

**Conclusion**

The frequency of PAD amongst people with type 2 DM was 27%. High density lipoprotein was markedly reduced among cases with PAD. The number of smokers in this study was low (5.6%) but 71.4% of diabetic smokers had PAD. Age did not influence the presence of PAD.

***Key Words;*** peripheral arterial disease, type 2 diabetes mellitus, ankle brachial index

**INTRODUCTION**

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycaemia due to absolute or relative deficiency of insulin affecting carbohydrate, fats and protein metabolism. The International Diabetes Federation atlas 10th estmates that about 537 million people worldwide aged 20 – 79 years are living with DM, 81% of whom reside in low medium income countries including Nigeria.[[1]](#endnote-1) In Nigeria, the South-South zone in Nigeria where Port Harcourt is located has the highest number with about 9.8% of people living with diabetes mellitus (PLWDM).[[2]](#endnote-2)

Diabetes mellitus results in chronic vascular complications including macrovascular complications such as peripheral arterial disease (PAD), coronary artery disease and stroke.[[3]](#endnote-3) These vascular diseases occur in clusters, when one is present the others are usually present.[[4]](#endnote-4) PAD results from narrowing of blood vessels with reduction in blood flow to the arms and legs (mostly). This results in ischaemic changes in the lower limbs and may ultimately cause ischaemic foot ulcers. PAD is common in people with type 2 DM and usually asymptomatic.[[5]](#endnote-5) Clinical examination including palpation of peripheral pulses may not correlate with the degree of PAD.[[6]](#endnote-6) The ankle-brachial index (ABI) assessment using a handheld doppler is an objective and sensitive method of diagnosing PAD in people with type 2 diabetes mellitus. ABI aids in eliciting findings of occult atherosclerosis and initiation of risk factor modifying therapies.[[7]](#endnote-7)

This study will determine the presence of PAD, its risk factors and indirectly assess other macrovascular complications among people with type 2 DM attending the medical outpatient clinic in University of Port Harcourt Teaching Hospital (UPTH). The aim was to determine the prevalence of PAD in people with type 2 DM attending University of Port Harcourt Teaching Hospital (UPTH).

**METHODS**

Recruited participants were assessed using a questionnaire and demographic information obtained. The body mass index (BMI) was determined. Samples were collected for fasting plasma glucose, glycated haemoglobin (HbA1/c) and fasting lipid profile. Fasting plasma glucose was performed using the glucose oxidase method. The Bio-Rad® high performance lipid chromatography (HPLC) machine was used to determine the HbA1/c, while fasting lipid profile was done using the Mindray BS-300 auto-analyzer. PAD was obtained by determining the ABI using a handheld Life Dopp® doppler. The right arm, right leg, left leg and left arm were assessed.

Data was retrieved and analyzed using Microsoft Excel® 2023 edition. Both categorical and numerical data were analyzed. Two by two contingency tables and Chi test were used to get the p-value for categorical data (e.g. sex and presence of hypertension). Numerical data (e.g. age, FPG, HbA1c, BMI, Lipid profile and ABI) were analyzed using various methods including student’s t-test and ANOVA. A *p*-value of <0.05 was taken to be statistically significant. Data were expressed as tables and charts.

**RESULTS**

One hundred and twenty-six cases with 100 controls were recruited into this study, making a total sample size of 226 participants. There were 58 females and 68 males in the cases (male-female ratio of 1.2:1), while the controls had 47 females and 53 males (male-female ratio of 1.1:1). The age of the cases ranged from 38 to 60 years with mean age of 52.5 ±5.6 years (females 52.8± 5.6 years, males 52.3± 5.7 years) and the controls had a range of 35 to 62 years with mean age of 50.2 ± 7.1 years (females 49.9 ± 7.4 years, males 50.5± 6.8years). The average BMI of the cases and controls were similar (cases 27.7 ± 2.6kg/m2, controls 26.8 ± 2.8 kg/m2).

Among the cases, 9 (7.1%) had no exposure to western education, 23 (18.3%) had a primary level of education, 34 (27%) had secondary level and 60 (47.6%) had a tertiary level of education or beyond. In the control group 22 (22%), 30 (30%) and 48 (48%) had primary, secondary and tertiary or post-tertiary level of education respectively.

**Table 1: *Fasting plasma glucose (FPG) and HbA1/c of the Cases and Controls***

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | CASES | | | CONTROLS | | | *p-Value* |
| *Mean* | *SD* | *Range* | *Mean* | *SD* | *Range* |
| FPG (mmol/L) | 7.0 | 1.8 | 3.9 – 14 | 4.5 | 0.8 | 2.5 – 6.3 | <0.0001\* |
| HbA1/c (%) | 7.6 | 1.3 | 4.5 – 11.2 | 5.2 | 0.7 | 3.5 – 5.7 | 0.009\* |

*FPG- Fasting Plasma Glucose, HbA1/c- Glycated Haemoglobin, SD- Standard Deviation,*

*\*Statistically Significant p-value*

The Doppler systolic pressure of the right and left brachial arteries in the upper limbs were the same with the dorsalis pedis and posterior tibialis bilaterally of the lower limbs in 24 (19%) of the diabetic group and 83(83%) of the controls; giving an ABI of 1. In the case group, 102 (81%) had ABI <1, 34 (27%) had ABI of <0.9 and 68 (54%) had ABI between 0.90 - 0.99. Among the controls, 17 (17%) had ABI <1 (range 0.91-0.99). None of the controls had an ABI of <0.9. *(See Figure* *1)*

**Figure 1: *Ankle Brachial Index of Cases and Controls (Based on Sex)***

ABI values grouped into 1, 0.9-0.99 and <0.9 (colour-coded)

*ABI\* Ankle Brachial Index*

Patients with diabetes and hypertension was seen in 25 (19.8%) of the cases and 15 (15%) of the controls. The average duration of hypertension in the PLWDM group was 6.16 years (±3.4) with a mean age of onset at 47.7 years (±3.7). The controls that were hypertensive had a mean age of onset at 47.1years (±4.2) and average duration of 6 years (±3). The diabetic patients with hypertension had a significantly higher mean HbA1c of 8.1%, compared to the people living with diabetes mellitus without hypertension with HbA1c of 7.5% (p= 0.036). The HbA1c in the people living with diabetes mellitus (PLWDM) and hypertension compared to the hypertensive controls was also significantly higher (8.1% vs 5.3%; *p*= <0.00001). The HbA1c in the control group with hypertension and without hypertension were 5.3% and 5.2% respectively.

People living with diabetes mellitus (PLWDM) and hypertension all had ABI of <1 ( right ABI 0.87, left ABI 0.87) which was significantly lower than the non-hypertensive PLWDM, right ABI 0.94, left ABI 0.94; p= 0.0001 and 0.0001 for the right and left ABI respectively. *(See Tables 2 & 3)*

**Table 2**

***Comparison of variables between the Cases with and without PAD***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variable | PAD Cases  (N= 34) | +/- SD | Cases without PAD  (N=92) | *+/- SD* | p-value |
| Age *(years)* | 52.5 | ***+/-*** *5.4* | 52.5 | ***+/-*** *5.7* | 0.97 |
| M/F Ratio | *1.6 : 1* | | *1.02 : 1* | | 0.29 |
| DM Duration *(years)* | 4.4 | ***+/-*** *2.4* | 5.1 | ***+/-*** *2.2* | 0.15 |
| FPG *(mmol/L)* | 7.3 | ***+/-*** *2* | 6.9 | ***+/-*** *1.7* | 0.39 |
| HbA1c *(%)* | 7.9 | ***+/-*** *1.4* | 7.5 | ***+/-*** *1.3* | 0.13 |
| Morisky Scale | 4.2 | *+/- 1.9* | 3.5 | ***+/-*** *1.5* | 0.07 |
| BMI *(kg/m2)* | 28.2 | ***+/-*** *2.7* | 27.6 | ***+/-*** *2.5* | 0.21 |
| ** HT Years | 6.3 | ***+/-*** *3.2* | 5.9 | ***+/-*** *3.2* | 0.78 |
| TCL *(mg/dL)* | 200.5 | ***+/-*** *30.7* | 193.7 | ***+/-*** *29* | 0.27 |
| LDL-C *(mg/dL)* | 118.8 | ***+/-*** *32* | 109.4 | ***+/-*** *32.2* | 0.15 |
| HDL *(mg/dL)* | 49.4 | ***+/-*** *9.1* | 53.3 | ***+/-*** *9.7* | 0.04\* |
| TGL *(mg/dL)* | 161.1 | ***+/-*** *23.6* | 154.7 | ***+/-*** *22.8* | 0.18 |
| Rt Arm *(mmHg)* | 141.4 | ***+/-*** *13.1* | 134.8 | ***+/-*** *11.9* | 0.01\* |
| Lt Arm *(mmHg)* | 140.7 | ***+/-*** *13* | 134.4 | ***+/-*** *12* | 0.02\* |
| Rt DP *(mmHg)* | 114.4 | ***+/-*** *19.5* | 130 | ***+/-*** *10.9* | <0.0001\* |
| Lt DP *(mmHg)* | 114.8 | ***+/-*** *19.3* | 130 | ***+/-*** *10.8* | <0.0001\* |
| Rt PT *(mmHg)* | 114.8 | ***+/-*** *19* | 130 | ***+/-*** *10.7* | <0.0001\* |
| Lt PT *(mmHg)* | 114.9 | ***+/-*** *19* | 129.9 | ***+/-*** *10.8* | <0.0001\* |
| Rt ABI | 0.81 | ***+/-*** *0.08* | 0.96 | ***+/-*** *0.33* | <0.0001\* |
| Lt ABI | 0.81 | ***+/-*** *0.08* | 0.97 | ***+/-*** *0.33* | <0.0001\* |

N- Number; M/F- Male/Female; BMI- Body Mass Index; DM- Diabetes Mellitus; FPG- Fasting plasma glucose; HbA1c- Glycated haemoglobin; HT- Hypertension; TCL- Total Cholesterol; LDL-C- Low density lipoprotein; HDL- High density lipoprotein; TGL- Triglycerides; Rt- Right; Lt- Light; DP- Dorsalis Pedis; PT- Posterior Tibialis; ABI- Ankle Brachial Index

*\*Indicates significant p-value*

**Table 3**

***Analysis of Variances between Cases with PAD, Cases without PAD & Controls***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | PAD Cases  (N=34) | Cases Without PAD (N= 92) | CONTROLS | p-value |
| Age *(yrs)* | 52.5 | 52.5 | 50.2 | 0.02\* |
| BMI *(kg/m2)* | 28.2 | 27.6 | 26.8 | 0.01\* |
| DM Duration *(yrs)* | 4.4 | 5.09 | 0 | 0.15 |
| FPG *(mmol/L)* | 7.6 | 6.9 | 4.5 | <0.0001\* |
| HbA1c *(%)* | 7.9 | 7.49 | 5.2 | <0.0001\* |
| HT *(N / %)* | 18 (52.9 %) | 7 (7.6 %) | 15 (15%) | <0.0001\* |
| HT years | 6.3 | 5.9 | 6 | 0.95 |
| TCL *(mg/dL)* | 200.5 | 193.7 | 193.9 | 0.52 |
| LDL-C *(mg/dL)* | 118.8 | 109.4 | 106 | 0.16 |
| HDL *(mg/dL)* | 49.4 | 53.3 | 56.4 | 0.0001\* |
| TGL *(mg/dL)* | 161.1 | 154.7 | 156.9 | 0.3 |
| Rt Arm *(mmHg)* | 141.4 | 134.8 | 141.4 | <0.0001\* |
| Lt Arm *(mmHg)* | 140.7 | 134.4 | 141.3 | <0.0001\* |
| Rt DP *(mmHg)* | 114.4 | 130 | 141 | <0.0001\* |
| Lt DP *(mmHg)* | 114.8 | 130 | 140.8 | <0.0001\* |
| Rt PT *(mmHg)* | 114.8 | 130 | 140.8 | <0.0001\* |
| Lt PT *(mmHg)* | 114.9 | 130 | 140.9 | <0.0001\* |
| Rt ABI | 0.8 | 0.96 | 0.99 | <0.0001\* |
| Lt ABI | 0.8 | 0.96 | 0.99 | <0.0001\* |

N- Number; BMI- Body Mass Index; DM- Diabetes Mellitus; FPG- Fasting plasma glucose; HbA1c- Glycated haemoglobin; HT- Hypertension; TCL- Total Cholesterol; LDL-C- Low density lipoprotein; HDL- High density lipoprotein; TGL- Triglycerides; Rt- Right; Lt- Light; DP- Dorsalis Pedis; PT- Posterior Tibialis; ABI- Ankle Brachial Index

*\*Indicates significant p-value*

The lipid profile of the PLWDM showed a mean total cholesterol value of 195.6mg/dL, LDL-C 112mg/dL, HDL 52.2mg/dL and triglycerides 156.4mg/dL. The control group had a mean total cholesterol, LDL-C, HDL and triglyceride values of 193.9mg/dL, 106mg/dL, 56.4mg/dL, and 156.9mg/dL respectively. The HDL in the controls was significantly higher than in the cases (p= 0.0002, <0.05). The LDL-C, total cholesterol and triglycerides between the cases and controls were comparable. *(Figure 2)*

**Concentration (mg/dL)**

**(mg/dL)**

**Figure 2: *Lipid Profile of Cases and Controls***

HDL- High density Lipoprotein, LDL-C- Low Density Lipoprotein

**Table 4**

***Pack years of smokers (Cases and Controls)***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cases |  | |  | Controls | |  |  | |
| Serial  No. |  | |  | **Serial**  **No.** | |  |  | |
| 4 | 5/20\*20 | | 5pk years | **3** | | 10/20\*10 | 5pk# years | |
| 34 | 10/20\*30 | | 15pk years | **20** | | 20/20\*15 | 15pk years | |
| 39 | 10/20\*20 | | 10pk years | **88** | | 10/20\*30 | 15pk years | |
| 51 | 20/20\*30 | 30pk years | | |  | | |  |
| 67 | 10/20\*30 | 15pk years | | |  | | |  |
| 98 | 15/20\*30 | 21.5pk years | | |  | | |  |
| 111 | 20/20\*25 | 25pk years | | |  | | |  |
| Mean pk years |  | **17.5pk years** | | |  | | | **11.7pk years** |

#pk- Pack

Out of the 126 cases, there were 7 (5.6%) smokers, 5 of them had PAD. Therefore 71.4% of the diabetic smokers had PAD. Of the 34 diabetic patients with PAD, 14.7% of them were smokers. There were 4 smokers in the control group. All the smokers in both the cases and control group were all males. The pack years for smokers is shown in 4.

**DISCUSSION**

This was a case-control study, involving people with type 2 diabetes mellitus (DM) and people without DM as controls. It set out to determine the prevalence and possible risk factors for peripheral arterial disease (PAD) in people with type 2 DM attending the University of Port Harcourt Teaching Hospital (UPTH).

Majority of the cases and controls had tertiary level of education. Some studies suggest that patients with a higher level of education (post-secondary) should have better glycaemic control,[[8]](#endnote-8), [[9]](#endnote-9) as they are more likely to understand and appreciate instructions and therefore have better motivation to achieve set out targets. In this study, we found an appreciable number of cases were not adherent to therapy. This may imply that because of the high level of literacy among our patients, the time given and quality of diabetic care education may be sub-optimal. Diabetic education is the pillar of optimal diabetic care.[[10]](#endnote-10) Good glycaemic controls may be achieved by tailoring therapeutic modules to ensure a normal life for the patient as much as possible. This therefore underscores the need for individualized care.[[11]](#endnote-11)

The average body mass index (BMI) of the cases and the controls fell into the overweight group of BMI classification, with 85.7% of the cases being overweight or obese. Cases in our study that had PAD had an average BMI of 28.24kg/m2, while cases without PAD had a BMI of 27.6 kg/m2. Being overweight or obese is a risk factor for type 2 DM. An increase in weight tends to result in increased insulin resistance which worsens glycaemic control and promotes vascular complications of DM, including PAD.

The target for people with type 2 DM is to have a BMI between 18 and 24.9kg/m2.[[12]](#endnote-12),[[13]](#endnote-13) The glycaemic control of the cases on the average was fair with an average fasting plasma glucose (FPG) of 7.0mmol/L. It is currently recommended that an individualized approach to glycaemic target should be the norm. It is agreed that tight glycaemic control is most beneficial if obtained early before complications have developed.[[14]](#endnote-14) The cases had higher values of dysplipidaemias with higher values of total cholesterol, triglycerides and low density lipoprotein (LDL-C), and significantly lower values of HDL-C than the controls. Dyslipidaemia is a common finding in people with type 2 DM.

PLWDM with an ankle brachial index (ABI) of <0.9 were diagnosed as having Peripheral Arterial Disease (PAD).[[15]](#endnote-15) This value is the most accepted value in most studies. The prevalence of PAD among the PLWDM was 27% with ABI range of 0.62-0.89. Several studies using ABI to detect PAD showa prevalence of 20 – 50%, depending on the population studied.[[16]](#endnote-16)[[17]](#endnote-17) However, a similar study by Oyelade et al showed a higher prevalence of 52.5% in PLWDM aged 50 – 89 years.[[18]](#endnote-18) This is not surprising as PAD increases with age, accounting for a higher prevalence in their study. Our study did not show a difference in age among the diabetic group with PAD compared to the diabetic group without PAD. None of the controls (including the hypertensive controls) had an ABI of <0.9. This shows that DM is a significant strong risk factor for PAD.

PLWDM who had PAD had a mean HbA1c value of 7.89%, while those without PAD had a mean value of 7.49%. This shows that the cases in this study had poor glycaemic control over the past 3 months. Elevated HbA1c increases the risk of microvascular and macrovascular complications in diabetes. This study shows that HbA1c had a weak negative correlation with PAD. Each 1% increase in HbA1c results in 18% increased risk of cardiovascular disease in type 2 DM patients.[[19]](#endnote-19), [[20]](#endnote-20) Hypertension is strongly associated with PAD.[[21]](#endnote-21) Hypertension results in endothelial damage, increased atherosclerosis, plaque formation with thrombi formation.[[22]](#endnote-22) These result in narrowing of the blood vessel. In patients with hypertension and type 2 DM, there is an exponential rise of cardiovascular risk. Our study supports this.

This study also showed that dysplipidaemia (increased total cholesterol, LDL-C and triglycerides with reduced HDL) was seen more in PLWDM with PAD than those without PAD. Dyslipidaemia is a risk factor for PAD.[[23]](#endnote-23) Insulin resistance and dysfunction of lipoprotein lipase results in dyslipidaemia seen in people with type 2 diabetes mellitus.[[24]](#endnote-24) The increased triglycerides, low density lipoprotein cholesterol and reduction in high density lipoprotein results in atherosclerosis with narrowing of the affected vessels which ultimately will result in PAD. Our study showed that HDL was significantly lower in PLWDM with PAD than those without PAD (p=0.04).

In this study, the overall number of smokers in our study was low (5.6%) but its contribution to PAD was noticeable. About 71.4% of people with type 2 diabetes mellitus that were smokers had PAD. Smoking is the most significant modifiable risk factor for PAD. The association of smoking and PAD was first documented over a hundred years ago. Smoking is said to increase atherosclerosis, with consequent narrowing of blood vessels and development of PAD.[[25]](#endnote-25)

Out of the 34 PAD cases, 8 (23.5%) of them were symptomatic, with a majority of 26 (76.5%) being asymptomatic. Our findings were similar to the findings in a study by Oyelade et al which found the prevalence of PAD to be 28.7% and that of asymptomatic PAD to be 71.3%. The fact that majority of the patients with PAD are asymptomatic emphasizes the need for PAD to be searched for objectively in patients at risk, especially patients with type 2 DM.[[26]](#endnote-26)

**CONCLUSION**

Diabetes Mellitus is the most common metabolic disorder resulting in morbidity and mortality. The care of the diabetic patient must be holistic, ensuring not only good glycaemic control but identifying modifiable risk factors that increase morbidity and mortality and preventing them. PAD is common among PLWDM and when present increases the risk not only for foot ulcers and amputations but also stroke and myocardial infarction.

Dyslipidaemia was common in our patients and when present is associated with vascular complications such as PAD. The prevalence of PAD amongst PLWDM from our study with an average age of 52.5 years was 27%. Hypertension is a risk factor for PAD and worsens the degree of PAD when present in PLWDM. Smoking was a major risk factor for PAD.

Disclaimer (Artificial intelligence)

Authors hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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