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Research Article

Assessment of Predictors and Prevalence of Peripheral Artery Disease among Type 2 Diabetic Patients in Zaria, Northern Nigeria -

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ABSTRACT

Background: The Ankle Brachial Index (ABI) is a simple, cheap, reliable, reproducible, highly sensitive and specific method used for the diagnosis of peripheral artery disease. It is defined as the ratio of the highest systolic blood pressure at the ankles divided by the higher of the systolic blood pressure at the arms.

Objective: To assess the predictors and prevalence of Peripheral Artery Disease (PAD) among type 2 diabetic patients in northern Nigeria.

Methodology: We conducted a descriptive cross sectional study among two hundred type 2 diabetic subjects comprising 82 (41%) males, 118 (59%) females and 100 age and gender matched non-diabetic, non-hypertensive, non-obese, non-cigarette smoker controls in Zaria, northern Nigeria. The mean ages of the diabetic subjects and the controls were 52.71 (± 10.60) and 52.10 (± 9.88) years respectively.

Results: The PAD among the type 2 diabetes subjects was 29% which was statistically significantly higher than the 13% in the controls (P = 0.00, OR = 2.76). Independent predictors of PAD after adjusting for confounders were intermittent claudication (AOR = 3.197), CI = 0.123-0.519), poor nails growth (AOR = 2.492, CI = 0.123-0.519) diminished/absent pedal pulses (AOR = 6.499, CI = 0.150-0.505), two hours postprandial glucose > 8.0 mmol/L (AOR = 2.512, CI = 0.032-0.264), HbA1c ≥ 7.0% (AOR = 2.589, CI = 0.064-0.477).

Conclusion: There is high (29%) PAD among type 2 diabetic patients in northern Nigeria. The routine use of ABI will be a very significant way for early diagnosis which may result in early treatment in order to prevent complications.

Keywords: Diabetic; Peripheral Artery Disease; Predictors And Prevalence; Zaria

INTRODUCTION

Peripheral Artery Disease (PAD) is a major macrovascular complication of diabetes mellitus which is usually diagnosed late especially in developing countries like ours due to absence of symptoms in the early phase and lack of routine screening, resulting in high rate of foot sepsis/gangrene with resultant amputations, poor quality of life and increased mortality. With the global epidemic of type 2 diabetes mellitus, a rise in the prevalence of peripheral arterial disease is expected.

Peripheral artery disease can be defined as obstructive arterial disease of the extremities that reduce arterial blood flow during exercise and in advanced stage at rest [1]. It affects about 12 - 14% of general population, 21% of the diabetic patients [2,3]. Results obtained from various studies, showed peripheral artery disease to be a very common complication of diabetes but most often asymptomatic [3-5].

The ankle-brachial pressure index is simple, cheap, reliable, reproducible, highly sensitive and specific method used for early diagnosis of peripheral artery disease [3-5]. It is calculated by dividing the systolic blood pressure at the ankles by the systolic blood pressure in the arms [3-5]. There still remained dearth of local studies on this subject in the northern Nigeria despite the high prevalence of diabetic foot ulcers/sepsis and non-traumatic amputations resulting from diabetes mellitus, hence, the need for this study which assessed the associations, predictors and prevalence of peripheral artery disease among type 2 diabetic patients in the region.

MATERIALS AND METHODS

We conducted a descriptive cross sectional study among type 2 diabetic patients and 100 non-diabetics, non-hypertensives, non-obese, non-cigarette smoker age and gender matched controls presenting consecutively to the endocrine outpatient and general outpatient clinics or on admission into medical wards within 13 month period ranging from November 2013 to November 2014 after obtaining ethical clearance from Ahmadu Bello University Teaching Hospital Health Research and Ethical Committee. Adequate counseling, informed consent and confidentially were applied throughout the course of the study.

Zaria is a prominent city in Nigeria being the seat of the famous Zazzau Emirate Council and the home of Ahmadu Bello University Teaching Hospital, Zaria which is the first Teaching Hospital in northern Nigeria. It has eight Federal Institutions of Higher learning with Nigerians of different cultural backgrounds and social class. So, the results of this study are likely a reflection of the national picture.

Exclusion criteria for the study were refusal to participate, presence of excruciating pains in the limbs as in cellulitis, painful active ulcers, pyomyositis, or deep venous thrombosis. Diabetes was defined by history of diabetes, on drugs for diabetes, repeated Fasting Blood Glucose or on the spot Random Blood Glucose ≥ 7.0 mmol/L and ≥ 11.1 mmol/L respectively. Hypertension was defined by history of hypertension, on antihypertensive medication or measured Blood Pressure ≥ 140/90 mmHg.

A validated physician administered Questionnaire was administered to obtain information including bio-data, current and past medical history. Physical examination findings including anthropometric measurements like body mass index which was calculated as weight in Kg divided by the square of the height in meters. Weight and height were measured in kilograms and meters respectively using the weighing scale produced by SECA, Inc, Germany along with waist and hip circumferences following WHO protocol [6,7]. Ankle-brachial index was measured using handheld Doppler manufactured by Summit Life Dop Inc, Chicago, USA, 7MHZ probe, lubricating gel and Mercury sphygmomanometer by Accousons.

Laboratory investigations done were Fasting Blood Glucose after 8-10 hours of overnight fast and 2 hours postprandial glucose at exactly 2 hours after meal by glucose oxidase method using strips from Chemelex Inc, Barcelona, Spain, HbA1c using Clover A1c, Korea reagent and machine. Fasting lipid profile after overnight fasting of 10-12 hours was done using Lipidpro strip, Inc, Korea. Qualitative variables such as gender, grading of obesity were presented as percentages, proportions and s while quantitative variable such as age, lipid profile, BMI were summarized using mean and standard deviation. Data was analyzed using SPSS version 17.0 (except chi-square for trend analysis that was performed using Epi Info version 7.0). Statistical test of significance at 0.05 alpha level was done using the chi-square to assess associations for the categorical variables. Significant *P*-value of less than of 0.004 was used for student 't' test after correction by Bonferroni method (in order to reduce the chances of false positive results following multiple tests) to compare means for the numerical variables. Multivariate logistic regression analysis was used to adjust for cofounders and obtain independent predictor of developing peripheral artery disease in diabetic patients.

Procedure for Measuring Ankle Brachial Index [8,9]

- The procedure was explained to the subjects and informed consent obtained (sometimes relatives, caregivers or interpreters were used to aid the individuals understand the issues surrounding the procedure).
- Tight clothing from both arms and stockings from both legs removed with cultural differences considered by inviting a family member to be present where necessary in order to maintain comfort and respect the individual's privacy and dignity. Active ulcers were well covered with sterilized dressings to prevent cross infections.
- Subjects were allowed to rest for 5-10 minutes in a supine position to reduce the effect of gravity on blood flow.
- An appropriate size sphygmomanometer cuff was used to record subjects' blood pressure following the procedure for the blood pressure measurement (inappropriate cuff size may lead to inaccuracy).
- After blood pressure measurement, the sphygmomanometer cuff was left in place, the brachial pulse was located at the medial third of the arm by palpation and ultrasound gel applied to the palpable site of brachial artery prior to measurement of brachial systolic pressure.
- Appropriate sized Doppler probe (8MHz) was used.
- The probe was angled at 45 - 60 degrees in the direction of the blood flow over the brachial pulse to detect a signal.
- The sphygmomanometer cuff was inflated until the signal disappeared, then, 30mmHg higher and deflated slowly until the signal returns in order to obtain brachial systolic pressure.
- The procedure was repeated with the other arm and the higher of the two values was recorded to calculate the ABI.
- Sphygmomanometer cuff was placed around the patient's ankle immediately above the malleoli as care was taken to avoid placing the cuff very high to avoid a false lower ankle blood pressure.
- Dorsalis pedis pulsation was palpated where possible at the dorsum of the feet between the proximal portions of the first and second metatarsal. Posterior tibial pulsation was palpated at just dorsal and medial to medial malleoli. If unable to palpate, ultrasound gel was applied and the pulsation located with Doppler probe signal.
- The cuff was inflated and the same procedure was repeated as for the arms to obtain systolic ankle blood pressure.
- The same procedure was repeated for the posterior tibial pulse and the other foot in order to reduce significant inaccuracy.
- Higher of the two values for each foot was used to calculate the ankle brachial index.
- ABI for each leg was calculated as follows:

Left ABI

- Higher of the left ankle systolic blood pressures divided by higher of the two brachial systolic pressures.

Right ABI

- Higher of the right ankle systolic blood pressures divided by higher of the two brachial systolic blood pressures.
- The lower ABI is the subjects recorded ABI and the results were explained to the subjects.

BMI < 18.5 Kg/m2 was considered underweight, 18.5-24.9 Kg/m2 - Normal, 25.0-29.9 Kg/m2 – Overweight,30.0-34.9 Kg/m2 – Grade 1 Obesity, 35.0-39.9 Kg/m2 – Grade 2 Obesity, ≥ 40.0 Kg/m2 Grade 3 Obesity. Waist Circumference ≥ 90 cm and ≥ 84 cm in males and females respectively were considered abdominal obesity. Waist to Hip Ratio ≥ 0.9 and ≥ 0.85 for males female were also classified abdominal obesity. Target Fasting Blood Glucose, Two Hours Postprandial Glucose, HbA1c, Total Cholesterol (TC), LDLc, HDLc, TG and TC/HDL ratio were 4.0-6.0 mmol/L, 4.0-8.0 mmol/L, < 7%, < 5.2 mmol/L, ≤ 2.6 mmol/L, > 1.1 mmol/L for males or > 1.3 mmol/L for females, < 5.0 respectively. 12 ABI was classified as 0.9-1.3 – Normal, 0.71-0.9 – Mild PAD, 0.41-0.7 moderate PAD, ≤ 0.4 – Severe PAD and > 1.3 - Non-compressible Vessels [7-9].

RESULTS

The 200 type 2 diabetic subjects consisted of 82 (41%) males and 118 (59%) females. The controls consisted of 46 males (46%) and 54 (54%) females. The mean ages of the diabetic subjects and the controls were 52.71 (± 10.60) and 52.10 (± 9.88) years respectively. No statistically significant difference. (*P* = 0.631). There was also no statistically significant difference in gender. (*P* = 0.241).

One hundred and forty diabetic subjects (70%) had hypertension, 27 (13.5%) had foot ulcers, 5 (2.5%) had previous amputation, 9 (4.5%) had previous stroke, 6 (3%) had chronic kidney disease but none was on dialysis. The predominant symptom of peripheral artery disease in the diabetic subjects was intermittent claudication in 23 (11.5%) of the diabetic subjects. Only one of the controls had each of intermittent claudication, rest pain and dystrophic nails.

Diminished/absent pedal pulse(s) was noted in 28 (14%), 30 (15.5%) had dried scaly skin, 29 (14.5%) had hair loss in the legs, 11 (5.5%) had foot ulcer, 1 (0.5%) had foot gangrene.

Among the diabetic subjects, 6 (3%) were underweight, 65 (32.5%) had normal BMI, 62 (31%) were overweight. Sixty-seven (33.5%) had general obesity with 41 (20.5%), 23 (11.5%) and 3 (1.5%) in grade 1, 2 and morbid obesity respectively. The mean BMI of the diabetic patients and the controls were 27.46 (± 6.07) Kg/m2 and 22.77 (± 3.85) Kg/m2 respectively. There was statistically significant difference. (*P* = 0.000).

One hundred and forty (70%) diabetic subjects had abdominal obesity assessed by waist circumference. Of these, 107 (76.4%) were females and 33 (23.6%) were males. The mean waist circumference of the diabetic subjects and controls were 93.65 (± 12.10) cm and 79.82 (± 7.73) cm respectively. There was statistically significant difference between the mean waist circumference of the diabetic subjects and that of the controls. (*P* = 0.000).

Among the diabetic subjects, 182 (91%) had abdominal obesity using the waist hip ratio. Among them, 107 (53.5%) were females and 75 (37.5%) were males.

The mean waist hip ratio of the diabetic and controls were 0.97 ± (0.41) and 0.88 (± 0.08) respectively. The mean waist hip ratio of the diabetic subjects was statistically significant higher. ($P = 0.000$).

The mean (± standard deviation) fasting blood glucose was 8.57 (± 4.50) mmol/L. Seventy eight (39%) diabetic subjects achieved target fasting blood glucose. The mean 2 hours postprandial glucose of the diabetic subjects was 13.0 (± 6.14) mmo/L. Only 38 (19%) achieved target level. The mean (± standard deviation) glycated hemoglobin was 9.94 ± 1.87%. Using the glycated hemoglobin, 192 (96%) of the diabetic subject did not achieve target level (Figure 1)

Among the diabetic subjects, 182 (91%) had elevated total cholesterol. The mean total cholesterol of the diabetic subjects and the controls were 6.57 ± (1.26 mmol/L) and 3.31 (± 0.66) mmol/L respectively. The mean total cholesterol of the diabetic subjects was significantly higher than that of the controls. ($P = 0.00$). One hundred and eighty two (91%) had elevated serum low density lipoprotein cholesterol. The mean LDLc of the diabetic and non-diabetic subject were 4.33 ± 1.41 mmol/L and 1.57 ± 0.65 mmol/L respectively. The low density lipoprotein of the diabetic subjects was statistically significantly higher than that of the controls. ($P = 0.000$).

One hundred and thirty (67%) of the diabetic subjects had reduced HDLc. The mean HDLc in the diabetic and control subjects were 1.29 ± 0.54 mmol/L and 1.32 (± 0.56) mmol/L respectively. The mean HDL of the diabetic was significantly lower. Seventy three (36.5%) of the diabetic subjects had elevated triglycerides.

The mean serum triglycerides of diabetic subjects and controls were 1.57 (± 0.94) mmol/L and 0.93 (± 0.42 mmol/L) respectively.

The mean serum triglycerides level of the diabetic subjects was statistically significant higher than that of the controls. ($P = 0.000$). Sixty–four percent had normal total cholesterol high density lipoprotein among the diabetic subjects. The mean total cholesterol high density lipoprotein ratio for the diabetic subjects and the controls were 4.91 (± 2.59 mmol/L) and 3.07 (± 1.80) mmol/L respectively. The mean TC: HDL ratio for the diabetic subjects was statistically significant higher ($P = 0.000$).

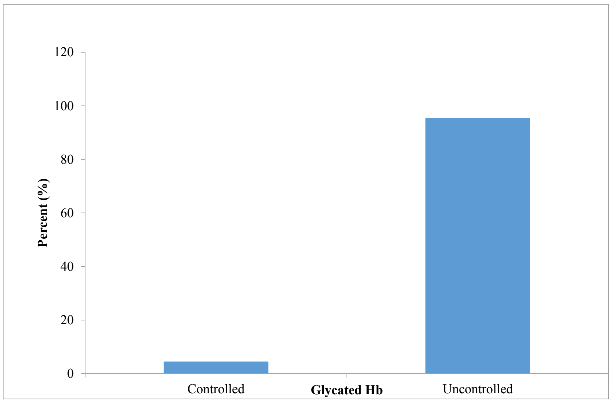

Figure 1: Glycaemic Control of the Diabetic Subjects

Table 1: Peripheral Artery Disease in the Diabetic Subjects and the Controls.

	PAD (%)	No PAD (%)	TOTAL (%)
Diabetics	58 (29)	142 (71)	200 (100)
Controls	13 (13)	87 (87)	100 (100)
Total	71	229	300

$X^2 = 3.84$, $P = 0.00$, OR = 2.76

The prevalence of peripheral artery disease in diabetic patients and the controls were 29% and 13% respectively (1).

There was a steadily increased in the prevalence in the prevalence among the diabetic subjects from 10% at 25 years to 33.3% at 54 years. Thereafter declined to 17.6% then increased suddenly to peak again (33.3%) at 65 years and above. There was no statistically significant association between advancing age and peripheral artery disease. ($P = 0.22358$). Twenty four (29.3 %) males and 34 (28.8%) females diabetics had peripheral artery disease. No statistically significant gender difference on the prevalence of peripheral artery disease. ($P = 0.53$). There was also no significant association between increasing duration of diabetes and peripheral artery disease. ($P = 0.243$).

After adjusting for confounding variables like advancing age, male gender, duration of diabetes, hypertension and dyslipidemia, intermittent claudication (AOR = 3.197, CI = 0.123 - 0.519), diminished/absent pedal pulses (AOR = 6.49, CI = 0.150 - 0.505), poor nails growth (AOR = 2.492, CI = 0.007 - 0.631), 2 hours postprandial glucose > 8.0 mm0l/L (AOR = 2.512, CI = 0.032 – 0.264) and HbA1c ≥ 7.0% (AOR = 2.589, CI = 0.064 – 0.477) were the independent predictors of peripheral artery disease among the type 2 diabetic patients.

DISCUSSION

The prevalence of peripheral artery disease in type 2 diabetic subjects of 29% being significantly higher than that of the controls (13%) and odd ratio of 2.76 was in keeping with earlier report that diabetic patients are 2 - 4 times more likely to develop peripheral artery disease when compared to the non-diabetics [10].

The explanation for the higher prevalence earlier reported in western Nigeria by Ikem et al (52.5%) and Oyelade et al (52.5%) were the high prevalence of foot ulcers (62.2%) and older diabetic subjects in the studies by Ikem et al and Oyelade et al respectively [10-12]. The prevalence of peripheral artery disease has been well known to increase with advancing and peripheral arterial is an important etiology of diabetic foot ulceration. The result of this study was similar to the findings of 24% and 39% in two different studies with similar inclusion criteria in Uganda [13-14].

The mean age of 50.2 ± 8.9 years was similar to the mean age 57 ± 12.3 years of diabetes in Nigeria observed by Chinenye et al in a multicenter study on profile of Nigerians with diabetes mellitus [15]. The presence of more females in this study (59%) in the diabetes subjects and 54% in the control subjects was the pattern observed in our diabetes clinic which has more females than the males. Similar observation was made in another study in southwestern Nigeria which enrolled 59% females [11]. This may be explained by the fact that females have more health care seeking behavior than their male counterparts [16].

The absence of significant association between peripheral artery disease and increasing age observed in this study was consistent with the findings of Mwebaze, Karaye [13,17]. However, studies by Ummuerri, Singh [18,19]. Showed significant association between peripheral artery disease and age. The lack of significant association in this study may be due to relatively small sample size compared to the above studies.

There was a steady rise in the prevalence of peripheral artery disease from 1-15 years and a sharp increase at 20 years and above, agreeing with the findings of Mwebaze, Ikem, Ummuerri et al that the prevalence of peripheral artery disease in diabetic patients increases with the duration of diabetes [11-13,18,19]. Not finding significant association may be due to markedly uneven distribution of the diabetic subjects by duration of diabetes with 80.5% of them being diagnosed within the previous 5–10 years.

The absence of significant association between peripheral artery disease and gender was similar to the reports of Mwebaze, Rabia [13,20]. Though peripheral artery disease was highly considered to be more common in males [18], the higher population of females in this study and the higher prevalence of abdominal obesity among female diabetics may explain the reason for no difference in gender prevalence. Also males are generally taller than females and therefore are likely to have greater augmentation of the ankle pressure by pulse wave reflection due to greater distance from the heart [21].

Hypertension, the most common cardiovascular disease was found to have no significant association with peripheral artery disease in this study. This was similar to the findings of. Mwebaze, Rabia, Paul [13,20,22]. Larger sample size might have shown association as persistent high blood pressure has been found to be a very important risk factor for peripheral artery disease in several studies [19,23,24].

The prevalence of peripheral artery disease was significantly higher among obese and overweight compared to normal and underweight diabetic subjects. Similar findings were reported by Ikem, Mwebaze [12,13,25]. This result was not unexpected as overweight and generalized obesity are very important cardiovascular risk factors. The lack of association observed by Oyelade et al may be explained by the older age groups in his study 7 as body mass index has been reported not to be a good a measure of obesity in the older age groups due to reduction in lean tissues, muscle mass and bone density [26].

Significantly higher prevalence of peripheral artery disease was observed in female subjects with abdominal obesity using waist circumference but not in males. Similar finding was reported by Lu [27]. No significant association was found between waist hip ratio and peripheral artery disease similar to the finding of a study in South Western Nigeria [28].

Uncontrolled HbA1c was found to be an independent predictor of peripheral artery disease. This agreed with the result of a meta-analysis of several studies by Sahin et al and UKPDS which showed independent association of poor glycemic control assessed by HbA1c and peripheral artery disease [29,30]. Prolonged hyperglycemia had been shown to accelerate the process of atherosclerosis by suppressing the activity of nitrous oxide synthase and increased elaboration of free radicals [31]. The significant association of postprandial glucose and peripheral artery disease observed can be explained by the fact that 2 hour postprandial glucose is an indirect measure of insulin resistance which is an important mechanism in the pathogenesis of peripheral artery disease in type 2 diabetes mellitus [32-34]. Similar findings of no associated between peripheral artery disease and fasting blood glucose was observed in this study were reported in a Ugandan and an Indian studies [13,35]. It may be that using fasting blood glucose alone does not predict the developing of long term complications in diabetic patients.

Dyslipidemia being a recognized risk factor for peripheral artery disease [30,36], showed no association in this study. Similar results were reported in a Nigerian study and other studies in Uganda, Malaysia, South African and Saudi Arabia [13,14,20,22,37]. Unlike coronary artery disease and cerebrovascular disease, the association of dyslipidemia and PAD appeared inconsistent. The very small number of smokers in this study explained why cigarette smoking was not found be associated with peripheral artery disease.

Screening of the diabetic subjects and the controls for Human Immunodeficiency Virus (HIV) would have added more value to this study considering the earlier report by Periard et al of higher prevalence of peripheral artery disease among HIV infected individuals than normal population [38]. The screening was not conducted because ethical consent for the test was not obtained.

CONCLUSION

PAD was found to be more common in diabetic patients. Most of them are asymptomatic. Independent predictors of peripheral artery disease in diabetic patients were poor glycemic control, intermittent claudication, diminished/absent pedal pulses and poor nail growth. Routine ABI will aid early diagnoses and treatment to prevent complications.

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