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Research Article

Associations of Carotid Atherosclerosis in Type 2 Diabetic Out-Patients in a Tertiary Health Facility in South-Eastern Nigeria: A Cross-Sectional Study

Chidiebele Malachy Ezeude[1, *], Afoma Marypaula Ezeude[2], Michael Chinweuba Abonyi[3], Henry Emeka Ikeabbah[4], Harriet Chinwe Nwadimkpa[5]

[1]Department of Internal Medicine, Nnamdi Azikiwe University, Awka, Nigeria
[2]Department of Nursing Sciences, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria
[3]Department of Internal Medicine, Enugu State University of Science and Technology, Enugu, Nigeria
[4]Department of Surgery, Nnamdi Azikiwe University, Awka, Nigeria
[5]Department of Internal Medicine, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria

Abstract

Background: Carotid atherosclerosis (CA) characterized by the thickening of the endothelium of the carotid arteries, is a reflection of generalized atherosclerosis and a surrogate for cardiovascular events. *Objectives:* To determine the prevalence and associated risk factors for CA in asymptomatic type 2 diabetes mellitus (T2DM) out-patients at NAUTH in Nnewi, Nigeria. *Materials and Methods:* This was a cross-sectional study that evaluated 142 T2DM out-patients. Relevant data was extracted with a researcher-structured questionnaire. Anthropometric measurements, glycated haemoglobin and fasting lipid profile were done. Carotid intima-media thickness was measured using ultrasongraphy. Ultrasonography of the brachial and pedal arteries was done using ultrasonic pocket doppler device and ankle brachial pressure index calculated. Lastly, the vibration perception threshold was determined using a digital biothesiometer. Data was analyzed using SPSS version 25. Results of categorical variables were presented in tables as frequencies and percentages. The mean values and standard deviation for the continuous variables were calculated. Chi-square test was used to assess the association between CA and categorical variables. The level of significance was set at $p < 0.05$. *Results:* The mean age of the 142 subjects was 59.15 ± 11.37 years and the gender distributions comprised 57.7% female and 42.3% male subjects, respectively. The prevalence of CA among the subjects was 49.3% and CA showed significant associations with educational level ($X^2 = 10.460$; $p = 0.015$), exercise status ($X^2 = 5.060$; $p = 0.024$), abdominal obesity in male ($X^2 = 4.659$; $p = 0.031$) and the female subjects, respectively ($X^2 = 8.874$; $p = 0.003$), and also with diabetic peripheral neuropathy (DPN) ($X^2 = 8.158$; $p = 0.004$). *Conclusion:* The prevalence rate of CA was high and depicted a huge burden of cardiovascular morbidities in T2DM subjects. Equally, CA showed significant associations with educational level, exercise, diabetic peripheral neuropathy and abdominal obesity in subjects.

Keywords

Associations, Carotid Atherosclerosis, Carotid Media-intima Thickness, South-East, Type 2 Diabetes

[*]Corresponding author: cm.ezeude@unizik.edu.ng (Chidiebele Malachy Ezeude), docchidi@yahoo.co.uk (Chidiebele Malachy Ezeude)

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1. Introduction

Diabetes mellitus (DM) is viewed as a metabolic disorder of multiple aetiologies, and is characterized by chronic hyperglycaemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action or both [1]. Diabetes is aetiologically classified into type 1, type 2, gestational DM and others [1]. Diabetes mellitus is approaching a pandemic level and constituting a healthcare burden globally. According to the International Diabetes Federation (IDF), an estimated 366 million people had DM globally with an estimated prevalence of 8.3% as of 2011 [2]. This figure is projected to hit 552 million by the year 2030, giving an estimated prevalence rate of 9.9% [2]. The geometric increase in the prevalence of diabetes and its complications places a heavy burden on the patients and the healthcare system [3]. Diabetes is now viewed as the modern public health scourge [4].

Carotid atherosclerosis (CA) is characterized by thickening of the inner lining of the arterial wall, referred to as the vascular endothelium. It is an important contributor to ischemic stroke and is a reflection of generalized atherosclerosis [5, 6]. Carotid atherosclerotic vascular disease (CAAD) is determined by an increased carotid artery intima media thickness (CIMT) and indicates patient at increased risk for fatal and non-fatal myocardial infarction [5].

Carotid duplex ultrasonography (CDUS) has proved to be very valuable in the evaluation and diagnosis of carotid atherosclerotic vascular diseases [7].

The intima-media thickness of carotid arteries is a surrogate marker for subclinical atherosclerosis in other vascular regions in the body and provides a noninvasive method for the risk assessment of cardiovascular and cerebrovascular diseases. It is associated with most risk factors for atherosclerosis [8, 9]. Ultrasound measurement of the CIMT is widely used as a measure of atherosclerosis in the evaluation for the presence of CAAD, its progression and possible regression with therapy [9]. It is a standardized international policy to measure the intima-media thickness (IMT) at the far wall of the artery, at least 5mm below or proximal to the carotid bifurcation so as to exploit the blood-filled lumen as an acoustic window for optimal visualization of the intima-media complex [10, 11]. The accuracy of the far wall intima-media thickness (IMT) measurement compares favourably with histological specimen as representing the true biological thickness of the vessel wall, while the near wall IMT measurement was shown to have a systematic measurement error because of the echogenicity of the adventitial layer masking the adventitial-medial boundary [12].

The traditional risk factors that had been shown to be associated with increased CIMT (carotid atherosclerosis) include older age, gender, educational level/western life style, hypertension, poor glycaemic control, dyslipidaemia and obesity [13, 14].

In Western Nigeria, Jinadu et al found that the mean CIMT was significantly higher in the diabetic subjects than in the non-diabetic individuals [15]. Similarly, in Western Nigeria, Okafor et al found a significant difference in CIMT of adult T2DM subjects compared to healthy non-diabetic adults, while Adekoya et al found that the CIMT among subjects with co-existing T2DM and hypertension was significantly higher (45.5%) compared to that of the controls [16, 17]. Adeleye et al found that the prevalence of increased CIMT (carotid atherosclerosis) was 53.7% among subjects with traditional cardiovascular risk factors (CVRFs), while Ayoola et al found that the prevalence of increased CIMT in children aged 12 – 17 years with type 1 DM was 40% [18, 19].

In Northern Nigeria, Ahmadu et al found that 62.5% of their diabetic subjects had no carotid artery stenosis while Baba et al found that up to 90.8% of T2DM subjects had high carotid atherosclerotic vascular disease (high CIMT) [7, 20]. In South-southern Nigeria, increased CIMT was higher among diabetic subjects (19.1%) than the non-diabetic controls (7.3%) [21]. Increased CIMT is significantly associated with increased duration of diabetes, hypertension and dyslipidaemia [15, 18, 20]. Equally, increased CIMT was found to be significantly correlated with glycated haemoglobin (HbA1c), age, fasting plasma glucose (FPG), systolic blood pressure (SBP), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) [20].

The burden of carotid atherosclerosis (CA) in Nigerians living with T2DM is very high and is still counting, just as diabetes mellitus is increasing geometrically. This unsavory trend notwithstanding, there is presently a dearth of published literature on this very vital topic in sub-Saharan Africa, especially in the South-eastern Nigeria. This study evaluated the prevalence of increased CIMT (CA), and its associations with the traditional cardiovascular risk factors (CVRFs) among the persons living with T2DM in Nnewi, South-eastern Nigeria. The cardiovascular risk factors evaluated by this study included: age, sex, educational level, DM duration, obesity, poor glycaemic control, hypertension, dyslipidaemia, non-alcoholic fatty disease (NAFLD), diabetic peripheral neuropathy (DPN) and peripheral artery disease (PAD).

2. Materials and Methods

This study was carried out at the diabetes out-patient clinic of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria. NAUTH is a referral hospital that covers Anambra State and the surrounding states in Southeastern Nigeria, including Imo, Abia, Delta, Enugu and Ebonyi States.

A total of 150 type 2 diabetes mellitus subjects who provided a written informed consent and were aged 18 years and above were recruited into the study from the outset. A total of

5 subjects dropped out of the study while 3 subjects had incomplete results and were not analysed. The final study population that was analysed was 142 subjects with type 2 diabetes mellitus. The study was carried out from June to December 2022. Ethical clearance for the study was obtained from the Research Ethics Committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi before the commencement of the study with the ethical code: NAUTH/CS/66/VOL.15/VER.3/077/2022/038.

The inclusion criteria for the study subjects included all consenting subjects with T2DM aged 18 years and above. The subjects were excluded from the study if they were less than 18 years of age, had type 1 DM, gestational diabetes mellitus (GDM) or were very sick.

2.1. Study Design

This was a cross-sectional, descriptive study. Subjects' recruitment into the study was via simple random sampling technique. The average number of T2DM subjects that attend the weekly diabetes clinic is about 40. The researchers got a total of 30 cards, wrote "yes" and "no" on 15 of the cards, respectively, then folded and put them in a pot. During each clinic day, each of the subjects with T2DM that met the inclusion criteria, had none of the exclusion criteria and gave a formal informed consent to participate in the study was made to blindly pick a card from the 30 cards in the pot. All the subjects that picked "yes" were recruited consecutively into the study. This procedure was repeated during each clinic consultation until the 150 subjects were recruited. No subject was allowed to pick a card on more than one (1) occasion throughout the duration of the study. The study was carried out in two phases and the researcher had two contacts with the subjects on two separate clinic days.

At the first contact, informed consent was obtained, a focused medical history was taken, anthropometric and blood pressure measurements were done. A pretested, researcher-structured and administered questionnaire was used for obtaining the subjects' relevant medical history and a study proforma was used for recording the results of the laboratory test results and clinical procedures. The questionnaire was translated to Igbo, in the local language by the researchers, for the subjects who were not educated enough to understand or communicate in English language. The duration of diabetes mellitus was taken as the period from the first diagnosis of DM to the time of the study. Next, bilateral carotid duplex ultrasonography scan (CDUS) was done to determine the carotid intima-media thickness (CIMT). Doppler ultrasonographic assessment of the brachial, and the pedal arteries were done, to determine the ankle brachial pressure index (ABPI) and biothesiometry was done to measure the vibration perception threshold (VPT).

2.1.1. Laboratory Procedure

At the second contact with the subjects, 5ml of venous blood was collected from each subject via venipuncture of the cubital vein following aseptic procedure. This was after they had observed a fast of about 8 - 14 hours based on the instructions they were given during the first meeting. 1 ml of blood from each subject was stored in ethylenediaminetetraacetic acid (EDTA) bottle and used for glycated haemoglobin (HbA1c) assay. The remaining 4 ml of blood was stored in plain bottle and used for fasting lipid profile assay. HbA_{1C} was measured using the boronate affinity chromatography method using the automated CLOVER A1c Analyzer (Infopia, Korea) and CLOVER A1c Self-Test Cartridge [22].

High density lipoprotein (HDL-C) was obtained by a precipitation technique [23].

Total cholesterol level was determined using the kit employing the enzymatic and the 4-hydroxybenzoate/4-ami\nophenazone systems (BioSystems) [24].

Triglyceride level was determined using a kit employing enzymatic hydrolysis of triglyceride with lipases (Randox) [25].

Low density lipoprotein cholesterol (LDL-C) was measured using a kit employing a precipitation technique (MyBioSource – MBS023682 kit. San Diego, California) [26].

2.1.2. Clinical Procedure

Carotid intima-media thickness was measured by an experienced radiologist at the NAUTH Radiology Department, using a MindRay DC-32 Diagnostic ultrasound system (Shenzhen, China, 2019) equipped with a curvilinear transducer (frequency 3.5 – 5 MHz). Carotid intima-media thickness was measured as the thickness of the double-line pattern of the far wall in a longitudinal image at right angle to the ultrasound beam, from the lumen intima interface to the media-adventitia interface; at the carotid bulb and common carotid artery at least 1cm proximal to the carotid bifurcation. This was done several times and an average taken on the right and left sides. Common carotid artery (CCA) IMT greater than 0.87 mm and internal carotid artery (ICA) IMT, greater than 0.90 mm were shown to be associated with a progressively increased risk of cardiovascular events [27].

Doppler ultrasonographic assessment of the brachial, dorsalis pedis and posterior tibial arteries were done, using EDAN SONTRAX Ultrasonic Pocket Doppler version 1.2 (CE 0123) with 8.0 MHz probe and an Accoson mercury Sphygmomanometer [28, 29]. Ankle brachial pressure index (ABPI) was calculated using the formular: ABPI for a leg = Higher pressure obtained from the ankle vessel in that leg / Higher systolic brachial pressure of the arms [30].

Peripheral artery disease (PAD) was taken as ABPI ≤ 0.9 [31].

The biothesiometer was used to objectively measure the vibration perception threshold (VPT), which was subsequently used for determining the presence of diabetic peripheral neuropathy in subjects. With the patient lying supine in a couch, testing was commenced by applying the vibrator of the biothesiometer to the pulp of the big toe of each foot.

The vibrator was steadily held, such that, its weight delivered a standard pressure on the vibrator button with the probe balanced vertically on the pulp of the big toe. The subject was instructed to concentrate fully on the procedure and to verbally report the first feeling of the vibration [32, 33]. The amplitude of the vibrator button was set as low as possible at the start of the testing and steadily increased until the subject perceived the vibration. The voltage the biothesiometer displayed at the instant of the vibration was recorded. The process was repeated thrice on the pulp of each of the big toes and the mean taken as the VPT for each of the lower limbs [32, 33]. Diabetic peripheral neuropathy was defined by a mean vibration perception threshold of> 25 Volts measured with the biothesiometer [32].

Weight and height were measured using Stadiometer (RGZ-120), waist circumference, measured with a measuring tape and blood pressure measured using Accoson mercury Sphygmomanometer in accordance with the WHO STEPS instruments [29].

2.2. Definition of Terms and Criteria

Hypertension was defined as systolic BP ≥ 140mmHg and or diastolic BP ≥ 90 mmHg, measured on at least 2 separate occasions or if a patient is already on anti-hypertensive medications [34].

Diabetes mellitus was defined by fasting plasma glucose of ≥ 7.0 mmol/l (126 mg/dl) measured on at least 2 separate occasions [1].

Type 1 DM was defined as subjects with DM who require daily administration as the sole treatment (are dependent on insulin) for survival and are at risk for ketoacidosis if insulin requirement was not met [1].

Type 2 DM was defined as patients with DM who are on diet therapy either alone or in combination with oral glucose lowering agent(s) with or without insulin for glycaemic control [1].

Dyslipidaemia was taken as HDL-C <1.04 mmol/L (males) or < 1.3 mmol/L or TG ≥ 1.7 mmol/L or LDL-C ≥ 2.6 mmol/L or total cholesterol (TC) ≥ 5.2 mmol/L or if the patient is on lipid lowering agents [35].

Young age was taken as 18-44 years, middle age as 45-64 years and old age as 65 years and above [36].

Poor glycaemic control was taken as $HbA_{1C} \geq 7.0\%$ [1].

Global obesity was defined by body mass index (BMI) >30 (kg/M^2) [1].

Central obesity was defined by waist to hip ratio (WHR) > 0.9 [1].

Carotid atherosclerotic vascular disease (CAAD) was defined by the common carotid artery (CCA) IMT greater than 0.87 mm and internal carotid artery (ICA) IMT greater than 0.90 mm [27].

Diabetic peripheral neuropathy (DPN) was defined by a vibration perception threshold (VPT) > 25 Volts measured with the biothesiometer [32].

Peripheral artery disease (PAD) was defined by an ankle brachial pressure index (ABPI) value of ≤ 0.9, while > 1.4 defined non compressibility of the arteries (calcification of the arteries) [28, 31].

2.3. Statistical Analysis

Data collected was entered into spreadsheet using Microsoft Office Excel, and then analysed using Statistical Package for Social Sciences (SPSS) version 25. Results of categorical variables were presented in tables as frequencies and percentages. The mean values and standard deviation for the continuous variables were calculated. Chi-square test or Fisher's exact test was used to determine the association between CA and the categorical variables. The level of significance for all tests was set at $p < 0.05$.

3. Results

3.1. Socio-demographic Characteristics

A total of 142 participants had complete results and were analysed in this study. The mean age of the subjects was 59.15 ± 11.37 years and they comprised 57.7% female and 42.3% male subjects respectively (details in Table 1).

Table 1. *Socio-demographic characteristics.*

Variable	Frequency	Percentage
Age (years)		
18-44	14	9.9
45-64	78	54.9
≥65	50	35.2
Mean = 59.15 ± 11.37		
Sex		
Male	60	42.3
Female	82	57.7

3.2. Prevalence of Carotid Atherosclerosis (CA)

The result showed that 49.3% of the participants had carotid atherosclerosis.

Table 2. *Prevalence of carotid atherosclerosis (CA).*

Variable	Frequency	Percentage (%)
Carotid atherosclerotic (CA)		

Variable	Frequency	Percentage (%)
Present	70	49.3
Absent	72	50.7

3.3. Association of CA with Socio-demographic CVRFs

Carotid atherosclerosis showed a statistically significant association with education level ($X^2 = 10.460$; $p = 0.015$) and exercise status ($X^2 = 5.060$; $p = 0.024$). Carotid atherosclerosis occurred more among the subjects who had a secondary (69.2%) and tertiary education (51.7%), respectively. Also, carotid atherosclerosis was seen among the subjects that exercised more (69.2%), compared to those subjects that did not. Other factors evaluated showed no significant association with carotid atherosclerosis ($p > 0.05$ in these cases) (details in Table 3).

Table 3. *Association between Carotid atherosclerosis (CA) and socio-demographic cardiovascular risk factors.*

Factor	CA		X^2	p-value
	Present	Absent		
Age (years)				
18-44	6 (42.9)	8 (57.1)		
45-64	34 (43.6)	44 (56.4)	3.540	0.170
≥65	30 (60.0)	20 (40.0)		
Sex				
Male	34 (56.7)	26 (43.3)	2.258	0.133
Female	36 (43.9)	46 (56.1)		
Marital status				
Single	0	0		
Married	68 (50.7)	66 (49.3)	2.002	0.157
Divorced	0	0		
Widowed	2 (25.0)	6 (75.0)		
Educational level				
No formal	2 (100)	0		
Primary	20 (35.7)	36 (64.3)	10.460	0.015
Secondary	18 (69.2)	8 (30.8)		
Tertiary	30 (51.7)	28 (48.3)		
Duration of Diabetes mellitus				
Short	20 (45.5)	24 (54.5)	0.376	0.540
Long	50 (51.0)	48 (49.0)		
Exercise				
Yes	18 (69.2)	8 (30.8)	5.060	0.024
No	52 (44.8)	64 (55.2)		

3.4. Association of CA with Clinical/Laboratory CVRFs

Coronary atherosclerosis showed a statistically significant association with abdominal obesity in both the male (X^2 = 4.659; p = 0.031) and the female subjects respectively (X^2 = 8.874; p = 0.003), and also with diabetic peripheral neuropathy (X^2 = 8.158; p = 0.004). A higher percentage of the subjects that had diabetic peripheral neuropathy (61.1%), also had carotid atherosclerosis. Other factors accessed showed no significant association with carotid atherosclerosis (p > 0.05 in these cases) (details in Table 4).

Table 4. *Association between Carotid atherosclerosis (CA) and clinical/laboratory cardiovascular risk factors.*

Factor	CA		X^2	p-value
	Present	Absent		
Abdominal obesity (males)				
Present	20 (71.4)	8 (28.6)	4.659	0.031
Absent	14 (43.8)	18 (56.3)		
Abdominal obesity (females)				
Present	26 (37.1)	44 (62.9)	8.874	0.003
Absent	10 (83.3)	2 (16.7)		
Global obesity				
Present	16 (40.0)	24 (60.0)	1.925	0.165
Absent	54 (52.9)	48 (47.1)		
Glycaemic control				
Good	16 (40.0)	24 (60.0)	1.925	0.165
Poor	54 (52.9)	48 (47.1)		
Systolic hypertension				
Present	24 (50.0)	24 (50.0)	0.014	0.905
Absent	48 (51.1)	46 (48.9)		
Diastolic hypertension				
Present	20 (47.5)	22 (52.4)	0.067	0.796
Absent	50 (50.0)	50 (50.0)		
Treatment for Diabetes				
Diet alone	0	0	1.955	0.376
OADs	50 (53.2)	44 (46.8)		
Insulin	4 (50.0)	4 (50.0)		
Both	16 (40.0)	24 (60.0)		
Non-alcoholic fatty liver disease				
Present	36 (47.4)	40 (52.6)	0.243	0.622
Absent	34 (51.5)	32 (48.5)		
Dyslipidaemia				
Present	64 (50.8)	62 (49.2)	1.004	0.316
Absent	6 (37.5)	10 (62.5)		
Antihypertensive use				

Factor	CA		X^2	p-value
	Present	Absent		
Yes	42 (52.5)	38 (47.5)	0.753	0.386
No	28 (45.2)	34 (54.8)		
Lipid-lowering drugs use				
Yes	46 (48.9)	48 (51.1)	0.014	0.905
No	24 (50.0)	24 (50.0)		
Diabetic peripheral neuropathy (DPN)				
Present	44 (61.1)	28 (38.9)	8.158	0.004
Absent	26 (37.1)	44 (62.9)		
Peripheral artery disease (PAD)				
Present	14 (53.8)	12 (46.2)	0.264	0.608
Absent	56 (48.3)	60 (51.7)		

4. Discussion

This study evaluated a total of 142 participants comprising 57.7% female and 42.3% male subjects, respectively, with a mean age of 59.15 ± 11.37 years. This study found that 49.3% of the participants had carotid atherosclerosis.

Adekoya et al found that the CIMT among patients with co-existing T2DM and hypertension was 45.5% which is slightly lower, but still comparable to the finding from the index study [17]. Both studies were done in Nigeria. Okafor et al found that the mean CIMT was significantly higher than that of healthy non-diabetic control subjects [16]. Okafor et al's finding also agrees with the index study that found a high prevalence of increased CIMT among type 2 diabetic subjects. Comparable to this study, Okafor et al studied more female subjects (59.3%) than male subjects (40.9%), but in contrast they analysed fewer number of diabetic subjects (108), with a younger mean age of 51.1 ± 11.1 years [16]. All the above research findings collectively tally with that of Klimontov et al, that carotid atherosclerosis was very common in subjects with T2DM and was associated with a high risk of cardiovascular events in this group of subjects [37]. Baba et al found that the prevalence rate of CIMT greater than 0.9 mm was 90.8%, and this was much higher than the prevalence rate of 43.9% found by this study [20]. Baba et al studied a lesser population of diabetic subjects (87) compared to this study (142) [20]. They equally studied more number of male subjects (51.7%) compared to the index study (42.3%). These could have accounted for the disparity in the findings of both studies [20]. A systematic review and meta-analysis found that men had greater CIMT compared to women [38]. Ahmadu et al found that 62.5% of their diabetic subjects had no carotid artery stenosis while Adeleye at al found that the prevalence rate of increased CIMT was 53.7% among subjects with traditional cardiovascular risk factors [7, 18]. Jinadu et al found that the mean CIMT was significantly higher in the diabetics than in the non-diabetics while Edafe et al found that prevalence rate of their T2DM subjects with increased CIMT was 19.1% [15, 21]. The prevalence rate of increased CIMT found by Edafe et al was far below that of the index study and some of the reasons for this difference could be attributed to the difference in the methodology adopted by the two studies: Edafe et al defined increased CIMT as that above 1.0 mm while the index study defined increased CIMT as the common carotid artery (CCA) intima-media thickness (IMT) greater than 0.87 mm and internal carotid artery (ICA) IMT, greater than 0.90 mm [27]. Equally, Edafe et al studied a smaller number of diabetic subjects (110) compared to the 142 studied by this study [21]. The mean age of the subjects from both studies was comparable at 54.85 ± 10.09 years and 59.15 ± 11.37 years by Edafe et al and the index study, respectively. Ayoola et al found that the prevalence rate of increased CIMT in children between the ages of 12 and 17 years with type 1 diabetes was 40% while Bulut et al found that CIMT was significantly higher in persons with impaired glucose tolerance compared to those with normal glucose tolerance or metabolism, showing that increased CIMT could even ante-date the diagnosis of diabetes mellitus [19, 39].

This study found a significant association between carotid atherosclerosis and increasing educational level, exercise, abdominal (central) obesity and diabetic peripheral neuropathy (DPN), Increased CIMT (carotid atherosclerosis) was more among subjects with secondary and tertiary education, compared to those with primary and non-formal education.

Equally, carotid atherosclerosis was seen more among the subjects that exercised more, the subjects that had abdominal obesity and those that had diabetic peripheral neuropathy. This study did not find significant association between Carotid atherosclerosis and other cardiovascular disease risk factors that included: age, duration of DM, sex, global obesity, glycaemic control, hypertension (systolic and diastolic), non-alcoholic fatty liver disease, dyslipidaemia and peripheral artery disease.

Most of the our educated subjects adopt western style of living, which includes sedentary living and consumption of high calories and weight-gaining diets, which are risk factors for cardiovascular events including atherosclerosis generally and CAAD, specifically. Also, most of our subjects that were exercising as at the time of this study, were those that were obese and had most of the other components of the metabolic syndrome, which itself is a conglomerate of the cardiovascular risk factors that are independently associated with increased CIMT [40-42]. This study found a positive association between increased CIMT and abdominal obesity. Farello et al, equally found earlier, that CIMT was increased in the obese subjects compared to the non-obese controls [43]. A study had earlier found that a 10kg increase in body weight, increased the risk of atherosclerotic coronary artery disease by 12% [44]. Obesity causes chronic inflammation which contributes to atherosclerosis and the pathophysiologic mechanisms involved, include the activation of adipokines/cytokines and increases in aldosterone levels the circulation [45]. The adipokines and cytokines activate and chemo-attracts monocytes/macrophages into adipose tissues that promote visceral adipose and systemic tissue inflammation, oxidative stress, abnormal lipid metabolism, insulin resistance, endothelial dysfunction, and hypercoagulability that contribute to atherosclerosis [45]. Increased aldosterone in the circulation expands the blood volume, promotes platelet aggregation, vascular endothelial dysfunction, thrombosis and fibrosis [45]. Hence, it is certain that obesity is a risk factor for cardiovascular diseases that include carotid atherosclerosis, coronary artery disease and peripheral artery disease either alone or as a component of metabolic syndrome [46, 47]. This effect of obesity occurs through its influence on known risk factors such as dyslipidaemia, hypertension, glucose intolerance, inflammatory markers, obstructive sleep apnea and prothrombotic state, in addition to yet to be recognized mechanisms [48].

This index study found a positive association between increased carotid atherosclerosis and diabetic peripheral neuropathy. Both disorders are end of results vascular atherosclerosis. Carotid atherosclerosis disease and diabetic peripheral neuropathy are surrogate markers for macro and micro angiopathies, respectively [49]. Avci et al more than a decade ago, found that carotid intima-media thickness was significantly increased in subject with diabetic peripheral neuropathy (DPN) compared to the subjects without that particular micro vascular complication of diabetes mellitus [49]. Also, a study found that CIMT showed a high predictive value for the presence of diabetic peripheral neuropathy [50].

Okafor et al found that the age of the subjects and plasma cholesterol level had positive correlation with CIMT, while Baba et al found that CIMT was significantly correlated with glycated haemoglobin (HbA1c), age, fasting blood sugar (FBS), systolic blood pressure (SBP), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) [16, 20]. Both Edafe et al and Jinadu et al found that CIMT was significantly associated with increasing duration of diabetes [15, 21]. Finally, Myasoedova et al found that men had greater CIMT compared to women [38].

5. Conclusion and Recommendations

This study found that the prevalence of carotid atherosclerosis among diabetic outpatients at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi in Southeastern Nigeria was high (49.3%), depicting a high burden of vascular events and its attendant morbidity and mortality in this group of subjects. Moreover, there was a significant association between carotid atherosclerosis and some cardiovascular risk factors that included abdominal obesity, diabetic peripheral neuropathy, exercise and educational level. These findings underscore the need for physicians to conduct regular and early screening of diabetic subjects for the presence of atherosclerotic vascular abnormalities and also, for timely institution of measures aimed at preventing and combating this abnormality, if it already existed. The measures that are effective are life style modifications; including medical nutrition therapy, exercise, shedding of excess weight for the obese subjects and pharmacologic interventions to address the risk factors for carotid atherosclerosis when they are indicated.

Abbreviations

CA	Carotid Atherosclerosis
T2DM	Type 2 Diabetes Mellitus
DPN	Diabetic Peripheral Neuropathy
CAAD	Carotid Atherosclerotic Vascular Disease
DM	Diabetes Mellitus
CIMT	Carotid Artery Intima Media Thickness
CDUS	Carotid Duplex Ultrasonography
IMT	Intima-Media Thickness
HbA1c	Glycated Haemoglobin
FPG	Fasting Plasma Glucose
SBP	Systolic Blood Pressure
TC	Total Cholesterol
LDL-C	Low Density Lipoprotein Cholesterol
HDL-C	High Density Lipoprotein Cholesterol
CVRFs	Cardiovascular Risk Factors

NAFLD	Non-Alcoholic Fatty Disease
DPN	Diabetic Peripheral Neuropathy
PAD	Peripheral Artery Disease
NAUTH	Nnamdi Azikiwe University Teaching Hospital
GDM	Gestational Diabetes Mellitus
ABPI	Ankle Brachial Pressure Index
VPT	Vibration Perception Threshold
EDTA	Ethylenediaminetetraacetic Acid
CCA	Common Carotid Artery
ICA	Internal Carotid Artery
PAD	Peripheral Artery Disease
WHO	World Health Organization
TG	Triglycerides
TC	Total Cholesterol
BMI	Body Mass Index
WHR	Waist to Hip Ratio

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Author Contributions

Chidiebele Malachy Ezeude: Conceptualization, Methodology, Original draft.

Afoma Marypaula Ezeude: Data curation, Data analysis, Review & editing.

Micheal Chinweuba Abonyi: Investigation, Resources, Validation.

Henry Emeka Ikeabbah: Project administration, Review & editing.

Harriet Chinwe Nwadimkpa: Supervision, Review & editing.

The authors read and approved the final manuscript.

Ethical Approval

Ethical clearance was obtained from the Research Ethics Committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi before the commencement of the study. A written informed consent was gotten from the study subjects before they were enrolled to participate in the study. Participation in the study was entirely voluntary and the subjects were allowed to withdraw at any point in the study, if they wanted, without any formal notification to the researchers.

Data Availability Statement

The data used to support the findings of this study would be made available by the corresponding author upon reasonable request.

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Conflicts of Interest

The authors declare no conflicts of interest.

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