Carotid Artery Intima-Media Thickness in Type 2 Diabetics and Non-Diabetics: A Case-Control Study

F O JINADU, E C NWOKORIE, T A OTTUN, A M OLUMODEJI

Citation

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Abstract

Background: Carotid intima-media thickness is a measure of the degree of atherosclerosis. We evaluated carotid intima-media thickness (CIMT) sonographically in individuals with type 2 diabetics and compared with values in normoglycemic controls.

Methods: This was a prospective case-control study that recruited 125 consenting confirmed type 2 diabetics (cases) and 125, age- and gender- matched, normoglycemic healthy controls over a 6-months period (October 2019 to March 2020) in the Lagos State University Teaching Hospital (LASUTH), Ikeja, Nigeria. Ultrasound determination of the carotid intima-media thickness was done in both cases and controls. The cases were recruited using systematic sampling method and the controls via convenience sampling. Data were presented in tables, scatter-plot graphs, and box and whisker plots. Pearson correlation coefficient was used to assess correlation between 2 continuous variables.

Findings: The mean age of the type 2 diabetics was 67.06±9.8 years while that of the non-diabetics was 66.98±10.7. The mean right CIMT was significantly higher in the diabetics (0.66 ± 0.1, $p<0.001$) than in non-diabetics (0.57±0.1). The mean left CIMT was significantly higher in the diabetics (0.67 ±0.1 $p<0.001$) than in non-diabetics (0.56±0.1). There was positive significant correlation of both right CIMT and left CIMT with the duration of type 2 diabetes mellitus (right CIMT, $r = 0.423$, $p<0.001$; left CIMT $r=0.175$, $p = 0.045$). Carotid plaques were significantly higher in the diabetics than non-diabetics (42.4% and 28.8% respectively $p=0.025$).

Conclusion: Type 2 diabetics had significantly higher CIMT and occurrence of carotid artery plaques than non-diabetics.

INTRODUCTION

Diabetes mellitus worldwide is projected to increase to affect 439million people by 2030.[1] Type 2 diabetics are prone to developing large artery atherosclerosis, stroke, and peripheral arterial disease with acute ischemic stroke being the leading cause of premature mortality and morbidity for men and women.[2,3] At least 20% of ischemic strokes are caused by carotid atherosclerosis.[4] Carotid intima media thickness (CIMT), a measure of atherosclerotic diseases, can be reliably determined by carotid ultrasound.[5]

Macro-vascular complications of diabetes are mainly represented by atherosclerotic disease, which develops over the course of 15 - 50 years and progress faster in patients with diabetes mellitus.[6,7] Early atherosclerotic disease is reflected by the carotid artery intima-media thickness (CIMT) which is the thickness between intima-lumina and media adventitia interfaces.[8,9] CIMT which is assessed on high resolution B-mode ultrasound has a normal range of 0.4mm to 0.8mm, and thickness > 1.5mm or encroaching at least 0.5mm into arterial lumen defines plaque.[10,11] The clinical significance of CIMT is that higher values are a marker of sub-clinical atherosclerosis.[12]

This study evaluated the carotid artery intima media thickness in individuals with type 2 diabetics and compared same with values in normoglycemic controls.

MATERIALS AND METHODS

This was a hospital-based, prospective, case-control study in the Lagos State University Teaching Hospital (LASUTH) over a 6 month period (1st of October 2019 to 31st of March 2020). The study population included consenting confirmed type 2 diabetics, recruited from the endocrinology clinic of the LASUTH, Ikeja, who met the inclusion criteria. The control group comprised of members of staff and general out-patient attendees who volunteered and met the inclusion criteria. Both groups were age and gender matched with an age matching factor of ±1.

The study inclusion criteria consisted of individuals with confirmed type 2 diabetes mellitus (as cases) and non-diabetics (as controls), who were non-hypertensive (blood pressure less than 140/90mmHg) and 18 years and above in age. Individuals with hyperlipidemia, known hypertensive (blood pressure ≥ 140/90mmHg), with history of use of oral contraceptives in the last 1 year, who refused to consent, with clinical evidence of heart failure or stroke, pregnancy, cigarette smoking, near occlusion of the carotid vessels, total occlusion of the carotid vessels or neck scars or wounds were excluded from the study. The controls who met the inclusion criteria were drawn consecutively at random from volunteers (members of staff of the hospital and general out-patient department attendees).

Technique:

Screening of the volunteers was done using Accu -Chek Active Glucometer (Serial Number. GB06183755, Art No. 0699377001). Any volunteer with a fasting blood glucose value equal or greater than 7.0mmol/L (126mg/dl) was excluded from the study. The participants BP was measured after 5minutes rest in a sitting position using Mercury Sphygmomanometer (Accoson, England) with appropriate cuff size. The BP was recorded in millimeter mercury (mmHg). Following overnight fasting, Accu- Chek Active Glucometer (Serial number GB06183755) with Accu-Chek active test strips was used to screen the controls for hyperglycemia under aseptic conditions.

A properly calibrated high quality universal portable weight scale was used to measure weights of all the participants in kilograms (kg) with light clothing and without shoes. The participants' height in meters (m) was measured without shoes; caps or head tie using a stadiometer with the participant in erect position and backing the rule. These measurements were documented in the study proforma. Body mass index (BMI) was calculated as weight/(height)[2.13] According to Truswell,[11] BMI was graded as: underweight (<18.50), normal weight (18.50-24.99), overweight (25.00-29.99), obese (≥30).

Carotid artery ultrasound scans:

Carotid artery scan was done using a high resolution General Electric Logiq C5 Premium machine (China, 2015) with a linear probe frequency range of 6-12MHZ with Doppler facility. This examination took an average of 35minutes per participant and each participant rested for 5-10minutes prior to the examination.

Participants removed anything that may interfere with the scanning like necklace, lie supine with their head slightly hyper-extended using pillow and neck rotated 450 away from the side under study to ensure adequate exposure of the neck. Acoustic gel was applied on the neck skin to remove air to ensure good ultrasound waves transmission.

On B-mode, the common carotid artery (CCA) was located lateral to the thyroid gland, medial to the internal jugular vein in the transverse plane above the clavicle and the linear probe was directed caudally to display as much of the CCA as possible. The probe was then rotated through 90^{o} into longitudinal plane to follow the artery distally until it bifurcates into internal carotid artery (ICA) posteriorly and external carotid artery anteriorly.

The probe was moved posteriorly and laterally to locate the ICA which was assessed in longitudinal and transverse planes. Pulsed Doppler scan in longitudinal plane was done after initial color Doppler assessment for the carotid arteries course and patency. The pulse repetition frequency (PRF) in pulsed Doppler, was the same as in color Doppler, and the lowest possible PRF without velocity aliasing was used.[14] Sample gate of 2-3mm was used. Optimal Doppler settings of gain, steer, focus, frequency and wall filter were employed with the angle of insonation less than 60[0.15]

Image Acquisition:

On placement of pulsed wave Doppler sample gate in the centre of vessel of interest with proper Doppler settings, the blood velocities were measured at 3 points 2cm proximal to the CCA bulb and 2cm above the bulb in the ICA. This was to avoid turbulent flow in the region of CCA bifurcation.

The CIMT was measured on a frozen, zoomed (magnified) image in the far wall of the CCA on both sides (figure 1) on a B-mode 1cm proximal to the carotid bulb at 3 points.[16] The mean of the CIMT was calculated and recorded.

Using modified Gray-Weale method,[17] carotid plaques were recorded and classified as:

Type 1-Uniformly anechoic or hypoechoic

Type 2-Predominantly (>50%) hypoechoic

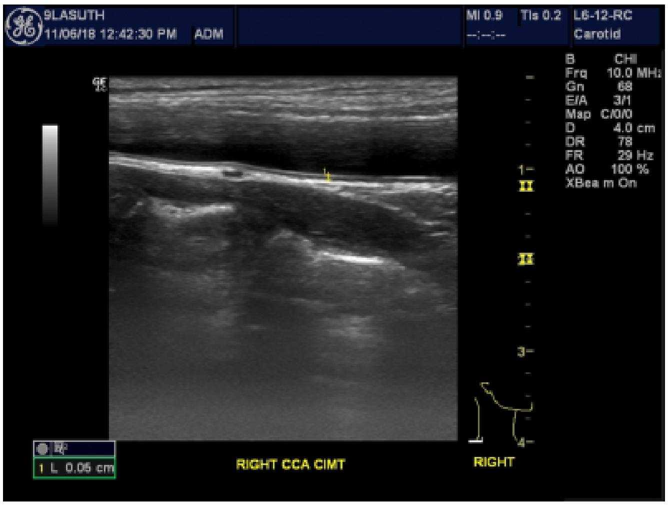
Type 3-Predominantly (>50%) hyperechoic

Type 4-Uniformly hyperechoic

Type 5-Uniformly echogenic with posterior acoustic shadowing (calcified plaque)

Figure 1

Longitudinal B-mode ultrasound image of the right CCA showing points (calipers) of measurement of CIMT at the far wall.



Data Entry and Analysis:

The demographic data, anthropometric measurements with ultrasound findings were analyzed using International Business Machines (IBM) statistical package for social science (SPSS) version 21 (New York, USA). Variables were presented in frequency, percentages, means and standard deviation. The mean of two continuous variables were compared using independent Student t-test and that of more than three variables using Analysis of Variance (ANOVA) F-test at 5% level of significance. Probability value (P-value) less than 0.05 was deemed significant. Data were represented in tables, bar charts, scatter-plot graphs and box and whisker plots. Pearson correlation coefficient was used to assess correlation between two continuous variables. Ethical approval was obtained from the Health Research and Ethics Committee of the Lagos State University Teaching Hospital.

RESULTS

One hundred and twenty five (125) consenting confirmed type 2 diabetics had common carotid artery ultrasound evaluation of CIMT. Males accounted for 46.4% of the study population while females were 53.6%. The majority of individuals in the study were in age group 60-69years (36.8%). Forty per cent of respondents were overweight (Table 1).

The CIMT on both sides were significantly higher in the male diabetics (Right $p<0.001$, Left $p<0.001$). The males also showed non-significantly higher CIMT on both sides in the non-diabetics (Right $p=0.502$, Left $p=0.495$). When age was considered, significantly higher CIMT was seen on both sides in the age groups 70-79 and ≥80 in the diabetics (Right $p<0.001$, Left $p<0.001$). A similar observation was also seen in the same age groups in the non-diabetics (Right $p <0.001$, Left $p<0.001$). The overweight had significantly higher CIMT on both sides in the diabetics (Right $p<0.001$, Left $p=0.009$). Similarly, the observations were the same for BMI in the non-diabetics (Right $p<0.001$, Left $p=0.009$) (Table 1).

The mean right CIMT was significantly higher in the diabetics (0.66 ± 0.1, $p<0.001$) than in non-diabetics (0.57 ± 0.1) (Figure 2). The mean left CIMT was significantly higher in the diabetics (0.67 ± 0.1 $p<0.001$) than in non-diabetics (0.56 ± 0.1) (Figure 3). Positive significant correlation of CIMT with body mass index ($p<0.001$) in the type 2 diabetics was seen (Figure 4). There was positive significant correlation of both right CIMT and left CIMT with duration of type 2 diabetes mellitus (right CIMT, $r = 0.423$, $p<0.001$; left CIMT, $r=0.175$, $p = 0.045$) (Figure 5 and 6).

Carotid plaques were significantly more present in the diabetics than non-diabetics (42.4% and 28.8% respectively $p=0.025$) (Figure 7). The type 3 carotid plaque was the predominant plaque in type 2 diabetics and non-diabetics while the type 1 carotid plaque was least present in both groups (Figure 8).

Table 1

Mean comparison of CIMT according to gender, age group and BMI in type 2 diabetics and non-diabetics

Variables (n, %)	Diabetics (125)		Non-diabetics (125)	
	Right	Left	Right	Left
Gender				
Male (116, 46.4)	0.71±0.1	0.72±0.1	0.58±0.1	0.57±0.1
Female (134, 53.6)	0.61±0.1	0.63±0.1	0.57±0.1	0.56±0.1
t-value	13.215	10.816	0.673	0.685
p-value	<0.001*	<0.001*	0.502	0.495
Age group (Years)				
40-49 (12, 4.8)	0.59±0.1	0.62±0.1	0.53±0.1	0.54±0.1
50-59 (46, 18.4)	0.62±0.1	0.62±0.1	0.55±0.1	0.55±0.1
60-69 (92, 36.8)	0.63±0.1	0.66±0.1	0.60±0.1	0.57±0.1
70-79 (88, 35.2)	0.70±0.1	0.72±0.1	0.62±0.1	0.59±0.1
≥80 (12, 4.8)	0.73±0.1	0.76±0.1	0.65±0.1	0.63±0.1
F-value	20.830	23.549	181.446	160.400
p-value	<0.001*	<0.001*	<0.001*	<0.001*
BMI				
Underweight (24, 9.6)	0.62±0.1	0.64±0.1	0.53±0.1	0.53±0.1
Normal (60, 24.0)	0.63±0.1	0.65±0.1	0.57±0.1	0.56±0.1
Overweight (100, 40.0)	0.68±0.1	0.69±0.1	0.59±0.1	0.57±0.1
Obese (66, 26.4)	0.66±0.1	0.68±0.1	0.59±0.1	0.57±0.1
F-value	6.061	4.075	8.511	7.291
p-value	<0.001*	0.009*	<0.001*	0.009*

*-significant p-value, t – Student t Test, BMI – Body Mass Index, F - One way ANOVA

Figure 2

t-value =14.187, p<0.001* Box and whisker plot illustrating mean comparison of right CIMT in type 2 diabetics and non-diabetics.

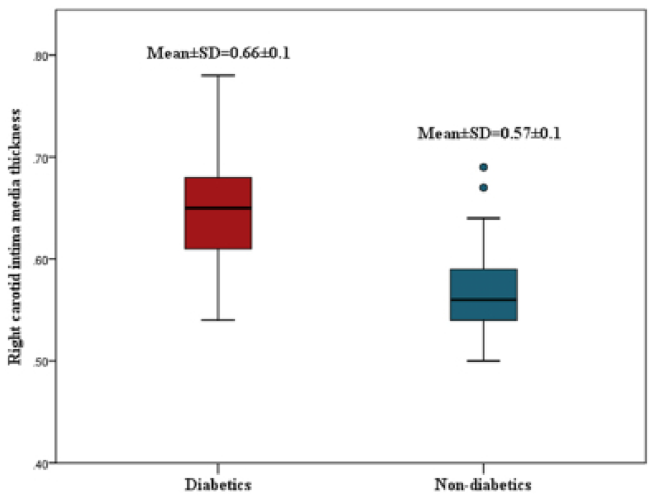


Figure 3

t -value = 18.621, p<0.001* Box and whisker plot illustrating mean comparison of Left CIMT in type 2 diabetics and non-diabetics.

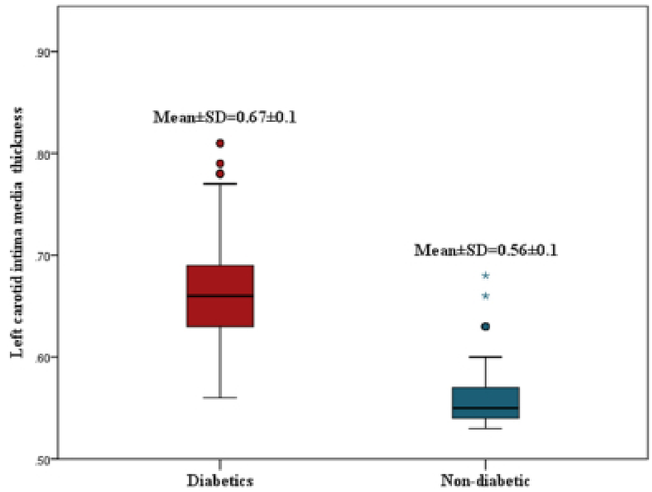


Figure 4

Pearson's correlation coefficient= 0.327, p<0.001* Scatter-plot graph illustrating association of CIMT with BMI in type 2 diabetics.

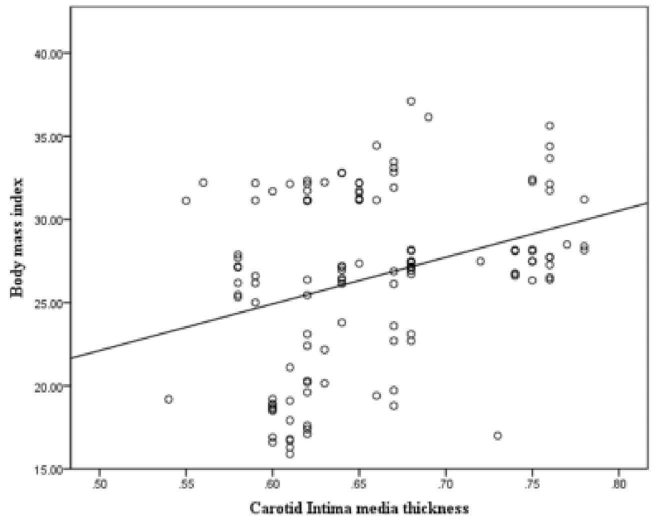


Figure 5

Pearson's correlation coefficient (r) = 0.423, p<0.001* Illustrating correlation of RT CIMT with duration of type 2 diabetes

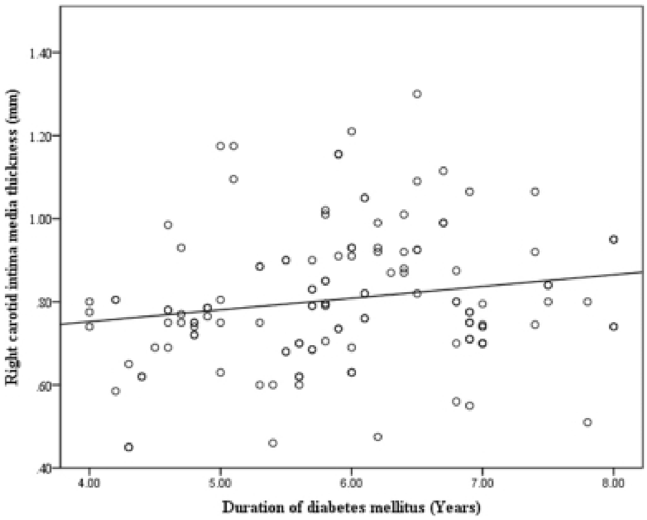


Figure 6

Pearson's correlation coefficient(r) = 0.175, p=0.025* Illustrating correlation of LT CIMT with duration of type 2 diabetes

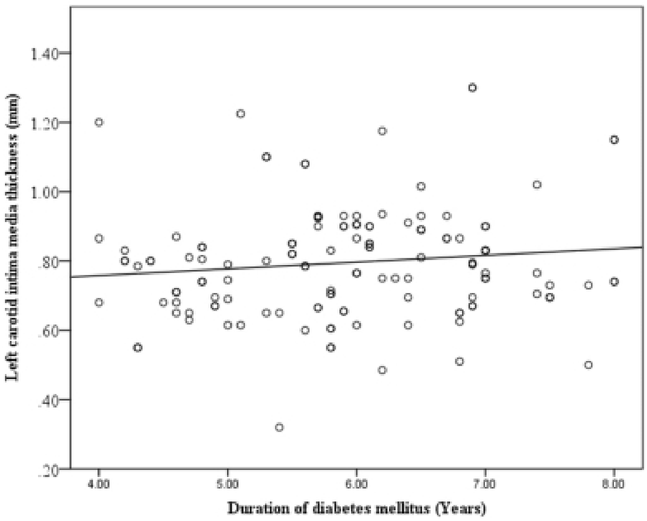


Figure 7

X2 =5.042, p=0.025* Bar chart illustrating frequency distribution of carotid plaques in type 2 diabetics and non-diabetics.

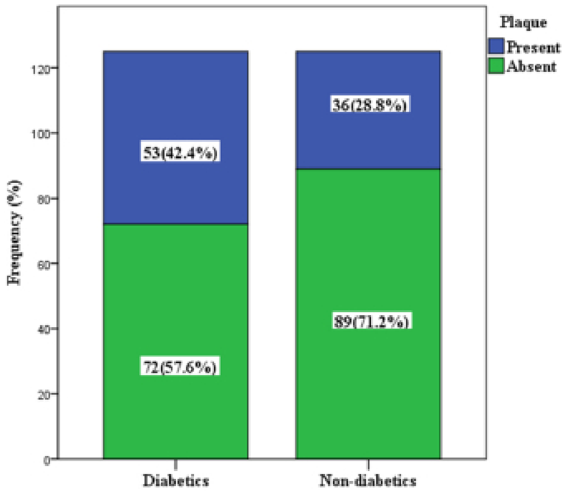
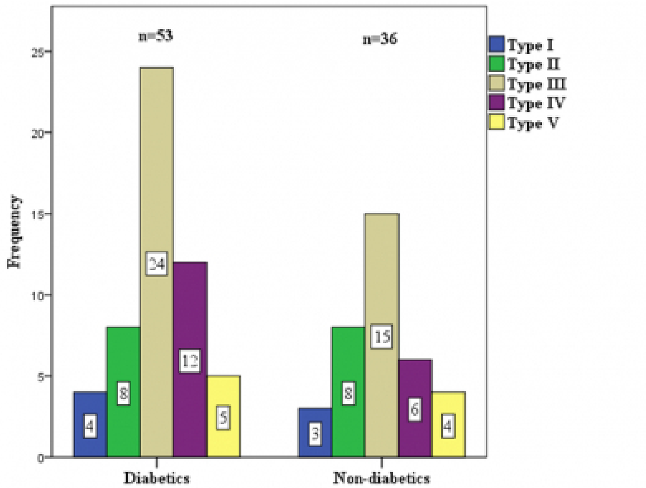


Figure 8

Frequency distribution of carotid plaque types in participants.



DISCUSSION

The carotid intima media thickness (CIMT) was significantly higher on both right and left sides in type 2 diabetics than controls. This is in concordance with the observations of Mohan et al[18] in India, Alizadeh et al[19] in Iran and Kota et al[20] in India, in their studies. However, Okeahialam et al[21] in a related study in Jos, Nigeria involving 211 individuals, found that CIMT was higher in type 2 diabetics, though not significantly. This finding is discordant with our observations. This difference may have been due to the technique of measurement used in their study. Okeahialam et al[21] measured a site at 1.0cm proximal to the carotid bulb whereas in this study, an average of three (3) points along 1cm proximal to the carotid bulb was used.

We found that carotid intima-media thickness increased significantly with age ≥ 70years in both diabetics and non-diabetics (P<0.001). This is consistent with the study done by Mohan et al[18] (P<0.001). Mohan et al found that carotid intima-media thickness increased significantly with age in the older age groups in type 2 diabetics and non-diabetics.[18] Similarly, Butt et al[22] in their study involving a total of 200 type 2 diabetics observed that beyond 70years, CIMT increased significantly with age. Butt et al also found a significantly higher carotid intima-media thickness in the males in the diabetics than non-diabetics (P<0.001).[22] This is consistent with findings from work done by Mackinnon et al,[23] in Western Germany involving 3,383 participants.

CIMT was also related to body mass index in the diabetics and non-diabetics and significantly higher carotid intima-media thickness was seen in both groups on the right and left in the overweight individuals (right P<0.001, left p= 0.009). This is consistent with the observation of Baba et al[24] in North Eastern Nigeria and Kotb et al[25] in Egypt. However, studies done by Güvener et al[26], in Ankara, Turkey and Kota et al,[20] in India, did not show any significant association of carotid intima-media thickness with body mass index in type 2 diabetics and non-diabetics. This variation could have been due to the smaller sample sizes in their studies or racial differences. Furthermore, Kota et al[20] used a different technique to measure CIMT. They measured carotid intima-media thickness at the proximal, mid and bulbal parts of the common carotid artery, whereas in this current study, average of the measurements along 1cm proximal to the common carotid artery bulb was used. Fennira et al[27] in their study in Tunisia involving 81 type 2 diabetics found out that carotid intima-media thickness was non-significantly increased with BMI in the diabetics (P<0.97). This variation with findings from our study would probably be explained by the relatively smaller sample size used in their study.

Furthermore, we observed that carotid intima-media thickness increased significantly with the duration of diabetes on both sides (right P<0.001, left P=0.045). This is in consonance with the studies done by Bashir et al[24] in Pakistan; Kota et al[20] in India; Butt et al[22] in Pakistan; and Bhosale et al[28] also in India.

Bosevski et al[29] in their study of 207 persons with type 2 diabetes in Australia found out that 41.8% of their study population had carotid plaques. This is similar with findings in this study that 42.4% of type 2 diabetics had carotid plaques. There was significantly higher carotid plaques in type 2 diabetics than non-diabetics (P=0.025) in this study, which is in concordance with the observations by Kota et al.[20]

In conclusion, carotid intima media thickness was significantly higher in type 2 diabetics than non-diabetics; significantly higher in the type 2 diabetic males, and increased significantly with age in the older age group. In the type 2 diabetics, CIMT showed significant positive correlation with BMI. Our findings in a Nigerian population lend credence to the contributory role of atherosclerosis in evolution of diabetic macrovascular complications.

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Author Information

Faosat Olayiwola JINADU
Department of Radiology, Lagos State University Teaching Hospital
Lagos, Nigeria

Emmanuel Chibueze NWOKORIE
Department of Radiology, Lagos State University Teaching Hospital
Lagos, Nigeria

Tawaqualit Abimbola OTTUN
Department of Obstetrics & Gynaecology, Lagos State University College of Medicine/Lagos State University Teaching Hospital
Lagos, Nigeria

Ayokunle Moses OLUMODEJI
Department of Obstetrics & Gynaecology, Lagos State University Teaching Hospital
Lagos, Nigeria