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Comparison of common carotid artery luminal diameter between adults with diabetes mellitus and healthy controls in North-eastern Nigeria

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Abstract

Background: Common carotid artery luminal diameter (CCALD) is used in epidemiological and interventional studies as biomarker of carotid atherosclerosis especially in subjects with DM. However, there are paucity of studies on the CCALD in subjects with DM in the study locality.

Purpose: This study is aimed at evaluating the CCALD in adults with DM differ from those of healthy controls

Methodology: Common carotid artery luminal diameters (CCALD) of 82 adult subjects with DM and 144 healthy controls were evaluated using a high-resolution ultrasound machine (Venue 50) equipped with electronic callipers and a linear array, high-frequency transducer (7-12 mHz). Measurements were taken at a point 1 cm distal to the carotid bulb.

Results: The overall mean CCALD was 6.12±1.47 mm and 5.88±0.77 mm for subjects with DM and healthy controls, respectively. The mean CCALD value is higher in subjects with DM compared to those of healthy controls though; there was no statistically significant difference in CCALD between the two groups. There were significant positive correlations between CCALD and age in male subjects with DM (r=0.488) while weak negative correlation exists in females (r=-0.073).Furthermore, weak negative correlation between CCALD and age among healthy controls (r=-0.117 and -0.020 for males and females, respectively).

Conclusion: The overall mean CCALD value in subjects with DM is higher than those of healthy control. The mean CCALD value is positively and significantly related to age in only male subjects with DM.

Keywords: Carotid; Artery; Luminal; Diameter; Diabetes mellitus; Ultrasound

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1. Introduction

Diabetes mellitus (DM)is a chronic metabolic disorder characterized by the prolonged presence of hyperglycemia due to defective insulin secretion, defective insulin action, or both (Goldenberg & Punthakee, 2013) and it is the major global human health challenge in the 21st century because of it high morbidity and mortality (Mohan, 2015). The global prevalence of DM is increasing steadily (Olokoba *et al*., 2012).

Generally, complications associated with DM are divided into macrovascular (stroke, coronary artery disease, and peripheral arterial disease) and microvascular complications, which include diabetic nephropathy, neuropathy, and retinopathy (Fowler, 2008).Macrovascular complications of DM are mainly represented by atherosclerotic disease, which develops over the course of 50 years and progresses faster in patients with DM (Paneni *et al.,* 2013).

Atherosclerosis is the progression of gradual constriction of the arteries through plaque formation within the artery wall (Bentzon *et al.,* 2014). Atherosclerotic complication of DM leading to stenosis with its attendant blood flow changes commonly affects carotid arteries (Saxena, et al., 2019). It is known that there is an association between ischemic stroke and carotid artery stenosis with diabetics being three times more likely to develop carotid stenosis than non-diabetics (De Angelis, *et al*., 2003).The prevalence of atherosclerosis increases exponentially with age, and elderly people have a higher risk of developing cardiovascular diseases (CVD) (Woo, *et al*., 2017).

The lumen of the coronary arteries dilates over-proportionally during early stages of atherosclerosis (Glagov 1987).Similar effects were observed for the carotid arteries which are the major blood supplier to the head and neck (Crouse et al 1994 & Crouse et al., 1996). Increased CCALD have also been independently related to numerous cardiovascular risk factors (Crouse et al., 1994). Accordingly, carotid dilation has been associated with incident cardiovascular events (Bots *et al.,* 2005 & Leone *et al*., 2008). Furthermore, recent studies have shown that CCALD was associated with a higher risk of any cardiovascular event and mortality, despite adjusting for other carotid parameters such as arterial stiffness and pulse wave velocity (Sedaghat, *et al.,* 2018).

Most of the information regarding the development and progression of atherosclerosis are obtained using conventional or computed tomographic angiography which are invasive, not readily available, accessible and affordable especially in a resource constrained developing nation like ours. However, the development of ionizing radiation frees, cheap, available and noninvasive imaging techniques such as the B-mode high-resolution carotid artery ultrasound provides a mechanism for studying the evolution of atherosclerosis including plaque characterization. Despite these developments, there is a paucity of literatures on B-mode ultrasound evaluation CCALD in adults with DM in the study locality. Therefore, this study is aimed at comparing the CCALD in subjects with DM and healthy controls.

2. Material and methods

A prospective study conducted over a period of four (4) months from 1st October 2021 to 31st January 2022 at ultrasound unit of the Maimusari Hospital, Maiduguri. The sonography of common carotid arteries of 226 subjects comprising 82 subjects with DM and 144 healthy controls attending general outpatient clinic were sonographically examined.Informed consent to participate in the study was obtained from all the subjects while documenting information on their age, disease conditions, disease history and lifestyle are being taken.

The subjects' height in metres (m) was obtained using a stadiometer with the patient standing erect and backing the scale. A weighing scale was used to measure weight (kg) and calculate body mass index (BMI), body adiposity index (BAI) and body surface area were calculated. Fasting blood sugar (FBS) level and blood pressure measurements were also obtained and recorded.

Non-probability (purposive) sampling method was adopted to recruit adult subjects with DM, while the healthy control subjects were recruited as volunteers.

2.1. Inclusion criteria

This study involved adult subjects between the ages of 18 and 80 years of age who had been diagnosed with DM (type 2) and consented to participate voluntarily. The healthy control subjects are consented individuals who are normotensive, non-diabetic, without the history of, renal diseases or any other disease condition that might affect the carotid artery. They were recruited from the general population and their age and gender distribution is similar to the case group.

2.2. Exclusion criteria

- Subjects that is less than 18 or greater than 80 years of age.
- Subjects with a known history of stroke, thyroid disease or any other complications affecting the kidney, brain, or heart.
- Pregnant women because of physiological changes and associated dilatation of the carotid artery during pregnancy.
- Subjects on anti-lipid prophylactic therapy or those with any other types of DM.

2.3. Sonographic examinations

Prior to the commencementof the examination, the researcher asked each participant to remove jewelleries and any other ornaments around the neck. The carotid artery was examined with the participant lying in supine position, right to the Sonographer/researcher on the ultrasound couch. The neck was hyper-extended (30^0) and placed on a small thick cylindrical foam pad to ensure adequate exposure of the neck depending on the subject's body physique. The head was then turned away from the examined side at about 45^0 from the midline to the opposite side. An ultrasound gel was applied to the antero-lateral aspect of the neck along the anterior border of the sternocleidomastoid muscle from the root of the neck to the base of the skull. This is to ensure proper transducer-skin contact and to reduce friction between the two surfaces. At the beginning of the examination, the carotid arteries were evaluated in B-Mode with appropriate optimizing factors.

The study protocol involved scanning the far wall and lumen of the right and left carotid artery which span from the superior aspect of the clavicle to the angle of the mandible while the internal jugular vein was used as a window as described in the previous study (Takiuch i*et al*., 2014). Sonograms of the carotid arteries were obtained for measurements using two antero-lateral scanning views (transversal and longitudinal) for each of the carotid artery. A transversal scanning view of the carotid vessel from the root of the neck to the carotid bulb and to the base of the angle of the mandible (C3 vertebra) was performed to localize any plaque.A transversal scanning view of the vessel with the transducer placed anterior border of the sternocleidomastoid muscle (1 cm below the carotid bulb) to measure the CCALD. A single measurement was recorded at each location for CCALD, which was taken as the distance between the leading edges of the lumen intima interface and the media-adventitia interface (second bright line) of the far wall.

All the sonographic examinations were performed using the 7-12 MHz, multi-frequency linear array transducer (contact area; 8mm x 28mm) of high resolution, touch screen, Venue 50 ultrasound machine (GE Medical System:2014, made in China) equipped with an electronic callipers. High-frequency transducer (vascular custom preset) was used because it gives a better resolution for superficial structures such as the carotid artery.

2.4. Statistical analysis

The quantitative variables are expressed as mean ± standard deviation, minimum and maximum values, while qualitative variables were presented as frequencies and percentages. The mean CCALD between subjects with DM and healthy controls; male and female subjects were compared using an independent sample t-test. While the mean values for the right and left sides were compared using a paired sample t-test. The association between theCCALD andcontinuous variables such the age, BMI, BSA, BAI, BP and FBS levels were calculated using univariate (Pearson's correlation coefficient). The data was analyzed using Statistical Package for Social Sciences (IBM SPSS]) Version 22.0. All the statistical tests were approved by assuming a null hypothesis of no difference, a $p \leq 0.05$ was considered statistically significant.

3. Results

The B-mode ultrasound examination CCALD was performed in all the carotid arteries of all the 226 subjects. The mean ± standard deviation of the subject's age was 46.04±12.6 years and 44.45±16.03 years for subjects with DM and healthy controls, respectively. There were 47(57.31%) males and 35(42.68%) females' subjects with DM, while healthy controls had 81 (56.25%) males and 63 (43.75%) females. There were more males than females in both subjects with DM and healthy controls. The predominant age group for both subjects with DM and healthy controls was age group 38-47 years (Table 1 and 2).

The overall mean CCALD for the subjects with DM and healthy controls were 6.12±1.47 mm and 5.88±0.77 mm respectively.The overall mean CCALD value in subjects with DM is higher than those of healthy control but the difference is not statistically significantas presented in table 3. The mean CCALD value for male and female subjects with DM was 6.24±1.80 mm and 5.96±0.86 mm respectively; the difference was not statistically significant difference (p=0.216).

Similarly, the mean CCALD for male and female in healthy controls was 5.98±0.83 mm and 5.75±0.67 mm respectively; there was a statistically significant difference (p=0.011).Generally,the mean CCALD values in males were higher compared to those of females in both subject groups as presented in tables 3 and 4.

In subjects with DM, the mean CCALD values for the right and left sides was 6.35±1.88 mm and 5.89±0.85 mm respectively, while in healthy controls, the mean CCALD for right and left sides was 6.05±0.79 mm and 5.71±0.24 mm respectively; the value is higher on the right side than on the left and the difference is statistically significant in both cases, as presented in table 5.

In subjects with DM, the mean CCALD values for age group 18-27 and >68 years was5.62±0.89 mm and 7.91±5.01 mm respectively (Table 6).The mean CCALD does not consistently increase with age in both subjects with DM and healthy controls (Table 6). There was strong positive correlation between age and CCALD in male subjects with DM (r= 0.488) and strong negative correlation with height (r=-0.445).There is no significant correlation between CCALD and any of the variables in healthy controls as presented in table 7.

In this study, carotid Plaques were seen in the common carotid artery (CCA) wall of 5 (6.10%) subjects with DM in this study, while only 1 (0.53%) was seen in the CCA of healthy controls. These plaques were more common in males (4) than in females and are more evident in the right CCA (3) than in the left.

Table 1 Age and sex distribution of the participants with DM

Age (years)	Male (n=47)		Female (n=35)		Total(n=82)	
	Frequency (%)	Mean ± SD	Frequency (%)	Mean ±SD	Frequency (%)	Mean ±SD
18-27	3(3.66)	22.33±2.15	1(1.22)	20.00±00	4(4.87)	21.75±2.36
28-37	9(10.97)	34.11±2.03	7(8.54)	34.14±2.34	16(19.51)	34.13±2.09
38-47	16(19.51)	41.31±2.55	15(18.29)	43.07±2.76	31(37.80)	42.16±2.76
48-57	10(12.19)	51.8±2.57	3(3.66)	50.00±00	13(15.85)	51.38±2.36
58-67	7(8.54)	62.43±2.99	6(7.32)	60.5±2.35	13(15.85)	61.54±2.79
≥68	2(2.44)	76.00±8.48	3(3.66)	71.67±2.89	5(6.10)	73.4±5.27
Total	47(57.32)	45.57±12.9	35(42.68)	46.56±12.4	82(100)	46.04±12.6

Table 2 Age and sex distribution of the healthy control participants

Age (years)	Male (n=81)		Female (n=63)		Total(n=144)	
	Frequency (%)	Mean ± SD	Frequency (%)	Mean ±SD	Frequency (%)	Mean ±SD
18-27	13(9.03)	24.54±2.5	9(6.25)	21.88±2.62	22(15.28)	21.68±2.50
28-37	10(6.94)	31.9±3.31	18(12.5)	33.72±2.42	28(19.44)	33.07±2.85
38-47	20(13.89)	41.05±2.21	18(12.5)	41.44±2.71	38(26.39)	41.24±2.43
48-57	8(5.56)	52.75±2.66	12(8.33)	51.58±3.11	20(13.89)	52.05±2.92
58-67	18(12.5)	62.28±2.21	4(2.78)	62.32±36	22(15.28)	62.23±2.4
≥68	12(8.33)	72.92±3.48	2(1.39)	80.00±00	14(9.72)	73.93±4.1
Total	81(56.25)	47.38±25	63(43.75)	40.90±13.20	144(100)	44.45±16.03

Table 3 Comparison of mean CCALD in subjects with DM and healthy controls

Measurements	Gender	Subjects with DM Mean±SD	Healthy controls Mean±SD	p-value
Mean CCALD (mm)	Male	6.24±1.80	5.98±0.83	0.110
	Female	5.96±0.86	5.75±0.67	0.064
Overall mean CCALD(mm)		6.12±1.47	5.88±0.77	0.133

A p-value of < 0.05 is considered significant

Table 4 Comparison of mean CCALD between male and female subjects with DM and healthy controls

Subjects	Males Mean±SD (mm)	Females Mean±SD (mm)	p-value
Subjects with DM	6.24±1.80	5.96±0.86	0.216
Healthy control	5.98±0.83	5.75±0.67	0.011*

A p-value of < 0.05 is considered significant

Table 5 Comparison of mean CCALD between right and left sides in subjects with DM and healthy controls

Subjects	Right Mean±SD (mm)	Left Mean±SD (mm)	p-value
Subjects with DM	6.35±1.88	5.89±0.85	0.003*
Healthy controls	6.05±0.79	5.71±0.24	0.000*

A p-value of < 0.05 is considered significant

Table 6 Mean CCALD (mm) value with age group in subjects with DM and healthy controls

Age group (Years)	Subjects with DM Mean±SD (mm)	Healthy controls Mean±SD (mm)
18-27	5.62±0.89	5.93±0.73
28-37	5.84±0.55	5.95±0.55
38-47	6.15±0.72	5.94±0.55
48-57	5.98±0.17	5.75±0.72
58-67	6.00±1.13	6.03±1.02
≥68	7.91±5.01	5.87±1.06

Table 7 Correlations between CCALD and some variables in subjects with DM and healthy controls

Variables	Gender	Subjects with DM		Healthy controls	
		R	***p***	***r***	***p***
Age (Years)	Male	0.488	0.001	-0.117	0.299
	Female	-0.073	0.678	-0.020	0.875
Height (m)	Male	-0.445	0.002	0.032	0.777
	Female	0.201	0.247	0.133	0.300

Weight (kg)	Male	-0.086	0.566	0.076	0.502
	Female	0.029	0.869	0.020	0.877
BMI (kg/m²)	Male	0.036	0.809	0.167	0.137
	Female	0.185	0.286	0.026	0.839
BSA (m²)	Male	0.000	1.000	0.115	0.307
	Female	0.012	0.943	0.019	0.882
BAI (%)	Male	0.132	0.378	0.025	0.825
	Female	-0.005	0.978	-0.030	0.815
SBP (mmHg)	Male	-0.118	0.429	0.062	0.585
	Female	-0.093	0.596	0.125	0.328
DBP (mmHg)	Male	0.186	0.211	0.045	0.691
	Female	-0.223	0.198	-0.083	0.516
FBS(mmol/L)	Male	0.076	0.613	0.085	0.451
	Female	0.074	0.675	0.146	0.253

Hint: BMI= body mass index, BSA= body surface area, BAI=body adiposity index, SBP=systolic blood pressure, DBP=diastolic blood pressure, FBS=body surface area.

4. Discussion

Diabetes mellitus (DM) may lead to changes in the morphology and function of the carotid arteries thereby increasing the prevalence and severity of carotid artery disease as well as poly-vascular diseases (Duprez *et al*.,2000; Katsiki & Mikhailidis 2020). Thickening of the carotid intima-media and luminal diameter enlargement is closely associated withthe morphological changes generally proceeding in tandem which produces a complex relationship between the two parameter sand atherosclerosis (Eigenbrodt *etal*.,2008). Blood vessels experience three primary mechanical forces: shear stress, the dragging frictional force created by blood flow, and tensile stress by circumferential stretch or tension and hydrostatic pressure (Gibbons, 1994; Trouub& Bark 1998).To maintain basal levels of stress, the intima of the blood vessel may thicken in response to reduced wall shear and to elevated tensile stress. In addition to these structural changes as wall thickening, long-term exposure to hemodynamic stimuli leads to functional vascular alterations as well (Kim *et al.,* 2016).

This study has revealed the role of ultrasound in the monitoring of complications associated with DM. Other studies had investigated CCALD in normal subjects documenting baseline values of normal CCALD in their study localities. However, this study compared the CCALD in subjects with DM and healthy controls and also correlated the CCALD with age, gender, BMI, BSA, BAI, BP and FBS levels.

The mean age of subjects with DM and healthy controls was 46.04±12.6, years and 44.45±16.03 years, respectively. The middle-aged population preponderance noted in this study was because of the fact that a majority of people with type 2 diabetes in developing countries are in that age range (Ahmadu *et al.,* 2012). In addition, most of the consenting subjects in this study fall within that age group. The increasing incidence of DM among these age groups is might be due to population growth, urbanization, obesity and physical inactivity (Sarah *et al*., 2004). There was also a male preponderance amongst subjects with DM and healthy controls in this study, which is in agreement with the earlier studies (Lundby-Christensen *et al.,* 2010; Baba *et al*., 2018).

The overall CCALD value was higher in subject with DM compared to those of healthy controls though, wasn't statistically significant. This finding is in agreement with the study by Kozaova*, et al* (2014) who reported a mean CCALD of 6.69±0.66 mm and 6.12±0.67 mm for DMand control subjects respectively. A similar finding has been reported byHenry *et al* (2015) who reported mean CCALD values of 6.31±0.92 mm and 6.13±1.06 mm for DM and control subjects respectively. Higher CCALD values observed in this study among subject with DM could be as a result of chronic exposure to higher glucose levels. This will lead to arterial stiffening, increases pulsatile load, and increases in CCALD. This impliesthat theinfluence ofhyperglycemia on the carotid wall is usually arteriosclerotic and that the glucose-related increase in carotid wall thickness might reflect atleast to ascertain the level, an adaptive remodelling aimed to mitigate increased pulsatile strain and preserve unchanged circumferential wall stress (Henry, *et al.,* 2015).

This study also found that the mean CCALD value on the right side was higher than that of the left side in both case and control groups and the differences are statistically significant. This finding is in agreement with those of Ahmadu *et al* (2018) and Gariepy *et al* (1993) who documented a similar finding in their separate studies.The main reasons for such variation between the two sides are not yet known.The left common carotid artery (CCA) is a direct branch of the thoracic aorta while the right CCA is a branch of the brachiocephalic artery which is a direct branch of the thoracic aorta. Hence, difference may have existed in arterial growth between two sides and/or that flow-mediated mechanical forces applied to the carotid wall also differ between the two sides.

In this study, mean CCALD value in males are higher than those of females in both case and control. However, the difference is only significant among healthy controls. These findings are in agreement with those of Denarie; *et al* (2000);Limbu *et a l*(2006);Ahmadu *et al* (2018),who in their separate studies reported higher CCALD values in malescompared to their female counterparts.None of the reviewed literatures reported. The precise reason for the variation between the two genders remained unclear. However, the possible reasons could be the frequent exposure of the male gender to psychological and environmental stress when compared to their female counterparts.

There was an inconsistent change in CCALD from age 18 to 80 years in both subjects with DM and healthy controls in this study. This finding is consistent with that of Ahmadu *et al* (2018).Strong and positive correlation between CCALD and age was noted in male subjects with DM this study. This implies that age does not play a cause significant change on the arterial wall because of compensatory remodelling.

5. Conclusion

This study revealed that the mean CCALD value in subjects with DM is higher than those of healthy controls. Age positively and strongly correlated with CCALD only among males with DM. High resolution ultrasound is a cheap, affordable, non-invasive, reliable, readily available and reliable imaging modality that is useful in monitoring DM including its complications.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed

Criteria of inclusion of Authors

All the authors conceived the idea of the topic. Alhaji Modu Ali and Anthony Chukwuka Ugwu conceived ideal of the topic and searched/ reviewed the relevant articles and drafted introduction and methodology, Mohammed Yusuf Mohammed and Umar Abubakar analyze the data and presented the result, Mohammed Ibrahim Abubakar and Umar Modu Kachallah drafted the discussion and conclusion. Alhaji Modu Ali drafted the abstract and all the authors reviewed and corrected the entire manuscript before submission.

Approval by authors

This manuscript was read and approved by all authors before submission

Statement of ethical approval

In line with the Helsinki Declaration, approval for this study was obtained from the Health Research Ethics Committee [HREC] of the Borno state ministry of Health.

Statement of informed consent

The consenting participants were thoroughly explained the procedure and both verbal and written informed consent was obtained from each of them before enrolling them into the study. They were made to be aware of their option to withdraw from the study at any point in time without losing any of the benefits or healthcare services rendered by the Hospital or the Centre.

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