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Sonographic Evaluation of Common Carotid Artery Intima-Media Thickness in Adults with Coexisting Type Two (2) Diabetes and Hypertension: A Case-Controlled Study

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Abstract

Diabetes mellitus (DM) and hypertension (HTN) are the two leading risk factors for atherosclerosis. Carotid intima-media thickness (CIMT) is considered a reliable surrogate measure for detecting subclinical atherosclerosis including its progression and regression. ***.*** *The study aim at evaluating the intima-media thickness of the common carotid artery in adults with coexisting diabetes mellitus and hypertension (DM+HTN) and compare with healthy controls.* ***.*** *A prospective case control study involving 115 adult subjects with coexisting DM+HTN and 144 healthy adult controls was carried out. Common carotid intima-media thickness (CCIMT) was measured at point approximately 1 cm distal to the right and left carotid bulb using the 7-12 MHz, multi-frequency linear array transducer of high resolution, touch Venue 50 ultrasound machine equipped with electronic callipers. The overall mean CCIMT was 1.13±0.40 mm and 0.82±0.23 mm for subjects with coexisting DM and HTN; and healthy controls, respectively. There was a statistically significant difference in CIMT of subjects with DM+HTN compared to healthy controls (p=0.000 each for both males and females, respectively). There were positive correlations between CCIMT and age in subjects with DM+HTN (r=0.260 and r=0.424 for males and females respectively); with healthy controls (r=0.619 and 0.626 for males and females, respectively). There was a statistically significant difference in CCIMT between subjects with DM+HTN and healthy controls. This implies that the increase in CCIMT is associated with both DM and HTN. In addition, age has a significant positive relationship with CCIMT in both subjects with DM+HTN and healthy controls.*

Keywords: Diabetes mellitus, hypertension, carotid, intima-media, thickness

INTRODUCTION

Diabetes mellitus (DM) and hypertension (HTN) constitute the greatest public health challenge to the entire world and both are important risk factors for coronary artery disease, heart failure, and cerebrovascular diseases (WHO, 2012). In addition, DM and HTN exert a significant burden to the teaming population resulting in increased morbidity and mortality, decreased life expectancy, and reduced quality of life, as well as individual and national income losses (Mohan, *et al*,, 2013). Currently, DM and HTN account for 48% and 3.5% of deaths from CVD, respectively (WHO, 2012). The overall burden of these diseases is greater in developing countries like Nigeria than in the developed world mainly due to ageing, lifestyle changes and the transition to a burden of chronic diseases (Amir *et al*., 2012).

Diabetes mellitus (DM) and HTN do co-exist, and this is on the increase worldwide (Berraho, *et al*., 2012). The co-existence of the duo had a prevalence rate of 71.6% in Nigeria is similar to 70.4% reported in Morocco (Berraho, *et al*., 2012 & Kayode *et al*., 2015). This increases chances of patients to develop both macrovascular and microvascular complications (Chobanian *et al*., 2003). This results increases the chances atherosclerotic related CVD related deaths (Chobanian *et al*., 2003).

Carotid artery Intima-media thickness (CIMT) is a surrogate measure of vascular atherosclerosis and represents vessel wall alterations over time caused by different risk factors (Grobbee & Bots, 1994). Sonographic assessment of the CIMT is a reliable, affordable, non-invasive and affordable imaging modality to assess atherosclerosis and atherosclerotic vascular diseases. Recently, considerable attention has been given to CIMT as an early indicator of atherosclerotic disease as a means of showing the effectiveness of medical therapies in treating atherosclerosis (O'Leary *et al*., 1996 & Uday *et al*., 2001). Sonographic imaging of carotid vessels can provide information on CIMT, wall calcification, presence of plaque and type which may indicate early arterial injury, hence, subclinical atherosclerosis. (O'Leary *et al*., 1996 & Uday *et al*., 2001) . There is paucity of local studies on carotid intima-media thickness in adults with both DM and HTN in the study locality and that is what prompted the researcher to embark on this study. Therefore, this study is aimed at evaluating the intima-media thickness of the common carotid artery in adults with coexisting diabetes mellitus and hypertension (DM+HTN) and compare with healthy controls.

Methodology

This is a prospective case control study conducted between 1st October 2021 and 31st January 2022 at ultrasound scan unit of the Maimusari Hospital, Maiduguri. The common carotid arteries of 259 subjects comprising 115 subjects with DM+HTN and 144 healthy control subjects attending general outpatient clinic were scanned. The sample size was determined using Fisher's statistical formular. Study was approved by the health research ethics committee of the state health ministry (058/2021). The subjects were informed about the nature and aim of the study and informed consent was obtained from each subject while taking information regarding 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+HTN, while the healthy control subjects were recruited as volunteers.

Inclusion/ exclusion criteria

The study included adult subjects between the ages of 18 and 80 years of age who had been diagnosed with DM+HTN and consented to participate voluntarily. The healthy control subjects are consented individuals who are normotensive, non-diabetic, without any 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.

The exclusion criteria include:

i. Subjects with a known history of CVA, thyroid disease or any other complications affecting the kidney, brain, or heart.
ii. Subjects who are pregnant women because of physiological changes and associated dilatation of the common carotid artery.

Sonographic examinations

Just prior to the commencement of the examination, the Sonographer/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 (Takiuchi *et al*., 2014).

Sonograms of the carotid vessels were obtained for measurements using two antero-lateral scanning views (transversal and longitudinal) for each of the carotid vessels. 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 longitudinal scanning view of the vessel with the transducer placed parallel to the anterior border of the sternocleidomastoid muscle to scan the vessels from the root of the neck to the skull base to measure the CCIMT. A single measurement was recorded at each location for CCIMT, 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 calliper. High-frequency transducer (vascular custom preset) was used because it gives a better resolution for superficial structures such as the carotid artery.

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 CCIMT between subjects with DM+HTN 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 the CCIMT and continuous variables such the age 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.

Results

The mean age of subjects was 56.38±12.49 years and 44.45±16.03 years for subjects with DM+HTN and healthy controls; respectively. There were 42 (36.52%) males and 73(63.48%) females' subjects with DM+HTN, while healthy controls had 81 (56.25%) males and 63 (43.75%) females. There was a predominance of females over males in subjects with DM+HTN (4:7) while there were more females among the healthy controls (4:3). The predominant age group for both subjects with DM+HTN was 48-57 years while for the healthy controls was 38-47 years (Table 1 and 2).

The overall mean CCIMT for the subjects with DM+HTN and healthy controls were 1.03±0.40 mm and 0.82±0.23 mm respectively. There was a statistically significant difference between the two subject groups (p=0.000) as presented in Table 3. The overall mean CCIMT for male and female in subjects with DM+HTN were 1.26±0.51 mm and 1.05±0.29 mm respectively; the difference was not statistically significant difference (p=0.000). Similarly, the mean CCIMT for male and female in healthy controls were 0.85±0.23 and 0.80±0.02 mm respectively; there was no statistically significant difference (p=0.056). The mean CCIMT values in males were higher compared to females in both groups as presented in Tables 3 and 4. In subjects with DM+HTN, the mean CCIMTs for the right and left sides were 1.08±0.31 mm and 1.17±0.46 mm respectively, while in healthy controls, the mean CCIMT for right and left sides were 0.81±0.22 mm and 0.85±0.24 mm respectively; there was a statistically significant difference observed between right and left sides in subjects with DM+HTN (p=0.000) and healthy controls (p=0.019), as presented in table 5.

In subjects with DM+HTN, the mean CCIMT for age group 18-27 and >68 years was 0.88±0.96 mm and 1.23±0.36 mm respectively. The CCIMT progressively increased with age in both subjects with DM+HTN and healthy controls. This increase was statistically significant in both subjects with DM+HTN and healthy controls. The CCIMT are higher in all age groups among subjects with DM+HTN compared with corresponding healthy controls. There was a positive correlation between age and CCIMTs in subjects with DM+HTN (r= 0.260 and 0.424 for males and females respectively) and healthy controls (r=0.619 and 0.626 for males and females respectively).

In this study, carotid plaques were seen in the common carotid artery (CCA) wall of 8 (6.96%) subjects with DM+HTN, while only 1 (0.53%) was seen in the CCA of healthy controls. These plaques were more common in males (7) than in females and are more evident in the left CCA (6) than in the right side.

Table 1: Age and gender distribution in participants with DM+HTN

Age (years)	Males (n=42)		Females (n=73)		Total (n=115)	
	Frequency (%)	Mean ± SD	Frequency (%)	Mean ±SD	Frequency (%)	Mean ±SD
18-27	1(0.87)	25.00±00	1(0.87)	22.00±00	2(1.74)	23.5±2.12
28-37	2(1.74)	32.00±5.66	5(4.35)	35.00±2.92	7(6.09)	34.15±3.63
38-47	3(2.61)	43.33±1.53	15(13.04)	42.93±2.46	18(15.65)	43.00±2.33
48-57	6(5.22)	53.17±3.43	25(21.74)	52.12±2.57	31(26.96)	52.32±2.73
58-67	14(12.17)	63.07±2.64	16(13.91)	61.44±3.10	30(26.09)	62.2±2.96
≥68	16(13.91)	70.06±2.93	11(9.57)	73.91±4.7	27(23.48)	71.63±4.14
Total	42(36.52)	60.57±12.09	73(63.47)	53.97±12.16	115(100)	56.38±12.49

Table 2: Age and gender distribution of the healthy controls

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 CCIMT in subjects with DM+HTN and healthy controls

Measurements	Gender	Subjects with DM+HTN Mean±SD	Healthy controls Mean±SD	p-value
Mean CCIMT (mm)	Male	1.26±0.52	0.85±0.23	0.000*
	Female	1.04±0.29	0.80±0.02	0.000*
Overall mean CCIMT (mm)		1.13±0.40	0.82±0.23	0.001*

A p-value of < 0.05 is considered significant

Table 4: Comparison of mean CCIMTs between male and female subjects with DM+HTN and healthy controls

Subjects	Males Mean±SD (mm)	Females Mean±SD (mm)	p-value
DM+HTN	1.26±0.51	1.05±0.29	0.000*
Healthy control	0.85±0.23	0.80±0.02	0.056

A p-value of < 0.05 is considered significant

Table 5: Comparison of mean CCIMTs between right and left sides in subjects with DM+HTN and healthy controls.

Subjects	Right Mean±SD (mm)	Left Mean±SD (mm)	p-value
DM+HTN	1.08±0.31	1.17±0.46	0.000
Healthy controls	0.81±0.22	0.85±0.24	0.019

DISCUSSION

Diabetes mellitus (DM) and HTN 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 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 and Mikhailidis 2020). Thickening of the carotid intima-media is closely associated with the morphological changes generally proceeding in tandem which produces a complex relationship between the two parameters and atherosclerosis (Eigenbrodt *et al*., 2008). Changes in both structural and functional aspects of arteries have been a research interest for several years as they are considered risk factors for cardiovascular events. Intima-media thickness changes due to impaired glucose levels (Hassan *et al*., 2016). Generally, arterial wall thickening may be in intima- media or muscular layer. As the carotid artery is elastic, the muscular layer is relatively small. Hence, the thickening of the carotid arterial wall is essentially due to intima-media thickening (Pignoil *et al.,* 1986). High-resolution ultrasound evaluation of carotid arteries is widely regarded as an accurate, affordable, doesn't involve the use of ionizing radiation, a non-invasive and available tool for screening and assessment of cardiovascular risks.

In this study, the mean age of subjects with DM+HTN and healthy controls was 56.38±12.49, 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 DM+HTN in developing countries are in that age range (Ayoola *et al*. 2015). The increasing cases of DM+HTN among middle age groups is probably due to population growth, urbanization, unhealthy life styles, obesity and physical inactivity(Sarah *et al*., 2004).

This study revealed that the overall mean CCIMT value was higher in subjects with DM+HTN compared to healthy controls and this difference was statistically significant. This finding is in agreement with the previous studies (Tawfeeq, *et al*., 2014; Mirza, *et al*., 2016; Regmi, *et al*., 2020; Shivaranjan & Mithun 2021, Adekoya, *et al*., 2022; Fatima, *et al*., 2022). These wide differences in the overall CCIMT in the two cohort groups were most likely due to higher blood pressure levels plus persistent hyperglycaemia in subjects with DM+HTN. The combined effects of increased blood pressure and oxidative due to chronic hyperglycaemia can cause injury to the endothelium of blood vessels and affect its function with subsequent thickening of intima-media complex via medial hypertrophy (Plavnik, *et al*., 2000; Tabit, *et al*., 2010). Both DM and HTN can independently increase CCIMT. On the contrary, values obtained for the two groups in this study are higher than those obtained from the previous studies reviewed (Tawfeeq, et al., 2014; Mirza, et al., 2016; Regmi, *et al*., 2020; Adekoya, *et al*., 2022; Fatima, *et al*., 2022). Only Shivaranjan & Mithun (2021) reported an overall mean value of 1.20±0.125 mm and 0.80±0.20 mm for DM+HTN and healthy control subjects respectively. These findings were slightly higher and lower for DM+HTN and healthy control subjects respectively compared to the current study. This difference in the mean CCIMT values might be due to the variations in race, sample size, duration of the disease, medication, measurement method employed, interobserver variability, study population, geographical location, cultural and economic settings. Determining factors such as the standard of living, lifestyle, nutrition, consumption habits, and health practices ultimately influence individual health status, and these same factors may have a role in the prevalence of DM and HTN and the global disparity in the documented CCIMT. Life style such as smoking has a significant impact on the CCIMT. A study by Shivaranjan & Mithun (2021) in India reported that CCIMT in DM+HTN subjects who are smokers (1.6±0.25 mm) was significantly higher than in DM+HTN subjects who are non-smokers (1.20±0.25 mm).

The mean CCIMT value in the left side was higher than the right CCA in both subjects with DM+HTN (1.17±0.46mm Vs 1.08±0.31 mm) and healthy controls (0.85±0.24 mm Vs 0.81±0.22 mm) studied. These findings are statistically significant in both groups (p=0.000 and p=0.019). This finding is in agreement with the previous studies (Hassan *et al*., 2016; Baba *et al*., 2018). The possible reason for such variations between right and left CCIMT is not yet clear. However, the left CCA is a direct branch of the thoracic aorta while right CCA originates from the division of brachiocephalic artery. Therefore, it is possible that differences have existed in the arterial growth between right and left sides and/or that flow mediated mechanical forces applied to carotid artery wall differ between the two sides (Clinton *et al*., 2008).

The mean CCIMT values in males are higher than those of females in both groups. Although, the difference is statistically significant only in subjects with DM+HTN. These findings are in line with the previous studies (Mohammed *et al*., 2020; Owoeye *et al*., 2017) and this might be explained by the gender difference in the development of atherosclerosis. These findings imply that the chance of developing atherosclerosis was higher in males compared to females, although the reasons for that remain unclear but may be due to the fact that males are more prone to psychological and environmental stress than females (Okeahialam *et al*., 2011).

There was a progressive increase in CCIMT from age 18 to 80 years in both subjects with DM+HTN and healthy controls in this study. The mean CCIMT values in both groups increases consistently with age. This finding is consistent with most of the previous studies reviewed (Okafor *et al.,* 2018; Shivaranjan & Somaiah 2021). Strong and positive correlation between CCIMT and age was noted in both groups in this study. The increase in mean CCIMT with age in healthy controls could probably be due to specific effect of aging on the arterial wall or probably be due to exposure to risk factor not measured or captured in this study. Higher CCIMT value with age among subjects with DM+HTN observed in this study could probably be due to the combined effect of chronic hyperglycaemia, prolonged high blood pressure and aging process on the intima media.

CONCLUSION

It was established from this work that there was a statistically significant difference in the CCIMT between subject with DM+HTN and healthy controls in this study. The mean CCIMT value in subject with DM+HTN is higher than healthy controls. Age, gender and blood pressure levels have a significant influence on the CCIMT in both groups. High resolution ultrasound is a cheap, affordable, non-invasive, reliable, readily available and reliable imaging modality that is useful in monitoring both DM and HTN.

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