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ORIGINAL RESEARCH

Carotid Doppler Ultrasonography in Patients with Co-existing Type 2 Diabetes Mellitus and Hypertension in Nigeria

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Abstract

Background: The co-existence of diabetes mellitus (DM) and hypertension (HTN) has been rising globally with subclinical atherosclerotic complications. These vascular changes can be detected using carotid ultrasonography.

Objectives: To determine and compare the carotid arterial structural wall changes and blood flow velocities of adults with co-existing DM and HTN with age- and sex-matched non-diabetic, non-hypertensive controls.

Methods: A cross-sectional comparative study of 300 participants comprising 200 adults with co-existing DM and HTN and 100 age- and sex-matched controls was done. Their carotid arteries were examined bilaterally for plaques, carotid intima media thickness (CIMT) and flow velocities - peak systolic velocity (PSV), end diastolic velocity (EDV), pulsatility index (PI) and resistive index (RI) using 4-12MHz linear array transducer. Visceral obesity and serum lipids were also assessed.

Results: The mean age of the subjects was 56.13 ± 6.93 years; they comprised 38% males and 62% females. The subjects' CIMT was statistically significantly higher ($p = 0.001$) with a three-fold mean increase (45.5%) compared to the controls (13.7%). Lower flow velocities but higher indices were also observed in the subjects. Strong and significant correlations were observed between EDV and PI ($r = -0.663, p = >0.001$), EDV and RI ($r = -0.661, p = >0.001$) and PI and RI ($r = 0.988, p = >0.001$) among the subjects.

Conclusion: Significant reduction in flow velocities with increased CIMT may be an early indication of subclinical atherosclerosis. Therefore, carotid ultrasonography should be mandatory in individuals at risk for early detection and possible prevention of atherosclerotic complications.

Keywords: Blood flow velocity, Carotid Intima Media Thickness, Carotid plaque, Hypertension, Subclinical atherosclerosis, Type 2 Diabetes mellitus.

Introduction

Framingham heart studies and epidemiology of cardiovascular diseases (CVD) reported hypertension (HTN) and diabetes mellitus

(DM) as major leading and metabolic risk factors for CVD, respectively.^[1] CVD ranks the highest cause of morbidity and mortality associated with non-communicable diseases, while HTN and T2DM rank among the leading CVD causes in developing countries.^[2,3] Presently, HTN and DM account for 48% and 3.5% of deaths from CVD, respectively.^[3] The high prevalence of T2DM and HTN in Nigeria could be attributed to rapid modernisation and globalisation of unhealthy lifestyles and ageing.^[4,5]

Hypertension and DM commonly co-exist, and this is on the rise globally.^[6] The prevalence rate of co-existing HTN and T2DM reported to be 71.6% in Nigeria is similar to 70.4% reported in Morocco.^[6,7] This co-existence increases patients' development and progression of macrovascular and microvascular complications.^[8] Additionally, their synergy with metabolic syndrome, which also frequently co-exist, increases CVD mortality through atherosclerosis.^[8]

Carotid ultrasonography (CU), an easily accessible, non-invasive validated imaging tool, is helpful in the identification and quantification of atherosclerotic burden.^[9] It identifies areas of increased wall thickness, carotid plaque, and flow velocity changes, which may represent early arterial injury, hence, subclinical atherosclerosis.^[9]

This study aimed to determine the prevalence of carotid atherosclerosis using ultrasonographic determination of carotid artery structural wall [CIMT and carotid plaques] and functional [blood flow velocity] changes in patients with co-existing T2DM and HTN. This study hypothesised that subclinical atherosclerosis via carotid artery structural and functional changes might be more apparent and grave in patients with co-existing T2DM and HTN than the non-hypertensive and non-diabetic controls.

Methods

Study design and participants' eligibility

This cross-sectional, comparative study was conducted over a year at the Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria. Two hundred adults aged 30-70 years with co-existing T2DM and HTN and 100 age- and sex-matched, non-diabetic, non-hypertensive controls were enrolled randomly from the Diabetes Clinic and General Out-patient Clinics. Excluded from the study were patients with Type 1DM, cerebrovascular accident, chronic kidney disease, coronary heart disease, and those who were pregnant or lactating. Patients with tracheostomy tubes, central lines, anatomical constraints like short, muscular necks, high bifurcation and tortuous artery were also excluded from the study.

The study was approved by the Health Research Ethics Committee of the hospital. Written informed consent was also obtained from the participants.

Procedures

An interviewer-administered, structured questionnaire was used to obtain demographic data, medical and social history, current medications, anthropometry, and clinical and laboratory parameters. The same ultrasound machine [4-12MHz linear array (PHILIPS® CLEAR VUE 550, Phillips Healthcare, 2014)] was used for all the study participants to exclude inter-equipment variation error. The same equipment was repeatedly calibrated and recalibrated to minimise inter-observer variability. Strict hygienic measures such as hand washing, use of latex hand gloves and equipment cleaning before and after each use were observed.

Anthropometry and clinical variables

Blood pressure was measured by the auscultatory method using appropriate-sized cuffs of Accuson® mercury sphygmomanometer. The blood pressure was measured in the sitting position following five minutes of rest; a mean of two brachial blood pressure measurements [systolic blood pressure (SBP) and diastolic blood pressure (DBP)] was recorded for each participant. Bodyweight in kilogram (kg) was measured

using a standing weighing scale (Seca® 755, Hamburg, Germany) on an even, horizontal hard surface. Height in meters (m) was measured using a stadiometer (Seca® 755, Hamburg, Germany) with the head in the Frankfort plane.^[10] The body mass index (BMI) in kg/m², was classified as underweight (BMI < 17.8), normal (BMI = 17.8–23.6), overweight (BMI = 23.7 – 26.8) and obese (BMI ≥ 26.9) in males and underweight (BMI < 17.8), normal (BMI = 17.8 – 25.6), overweight (BMI = 25.7 – 28.7) and obese (BMI > 28.8) in females.^[11] The waist circumference (WC) in centimetres (cm) was measured using the WHO STEPS protocol.^[12] It was classified as normal (WC < 82.99cm), overweight (WC = 83–94.99cm) and obese (WC > 95cm) in women and normal (WC < 83.99cm), overweight (WC = 84–95.99cm) and obese (WC > 96cm) in men.^[13]

Laboratory evaluations and definitions

Venous blood samples collected aseptically between 07:00 Hours and 08:00 Hours after an overnight fast were assayed for glycosylated haemoglobin (HbA1c), fasting blood glucose (FBG) and serum lipids. Two millilitres (ml) of blood were dispensed into fluoride oxalate and ethylenediamine tetra-acetic acid (EDTA) bottles for glucose and HbA1c estimation, respectively. Three millilitres of blood were also dispensed into a plain sample bottle for lipid assay. Plasma samples for FBG were analysed immediately, and HbA1c samples were assayed within 1 hour with a Clover HbA1c analyser manufactured by Infopia® Co. Ltd, South Korea. The venous blood for lipid assay was centrifuged (swing-bucket) within two hours of collection at 3000 revolutions per minute (RPM) for five minutes. The separated serum samples in plain plastic screw-capped containers were stored frozen (–20°C) and assayed for serum lipids within one week.

Samples were analysed at the hospital's Research Laboratory by a Consultant Chemical Pathologist. Colourimetric kits supplied by Randox Laboratories Ltd, United Kingdom, were used to estimate FBG, total cholesterol

(TC), triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) assay. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula.^[14] Other laboratory definitions included the following: HbA1c (normal <6.5%),^[15] FBG (normal 70–100mg/dl)^[16] and fasting lipid profile [TG < 200mg/dl, TC < 200mg/dl, LDL-C < 160mg/dl and HDL-C > 40mg/dl].^[16]

Ultrasound assessment

The CIMT is the distance of the leading edge of the first hyper-echogenic line (lumen-intima interface) from the leading edge of the second hypo-echogenic line (media-adventitia interface) of the carotid artery.^[17] (Figures 1 and 2). Carotid plaques are focal arterial luminal encroachment of at least 0.5mm, 50% of the surrounding intima-media thickness or a thickness ≥ 1.4mm when measured from media-adventitia interface to the intima interface.^[18] Two radiologists with five years of experience in CU concurrently performed the ultrasonography of the participants, each blinded to the result of the other. The participants were positioned supine, with jewellery and clothing removed from the study area. The chin was slightly extended, head rotated 45° away from the examined side per time after applying a clear warm water-based ultrasonic gel. Scanning started from the common carotid artery (CCA), followed by the carotid bulb (CB) and internal carotid artery (ICA) in sagittal planes bilaterally. Three measurements of CIMT at the far wall, 0.5cm apart, were obtained at the bulb, 1cm below and above the bulb for CCA and ICA bilaterally. Left and right CIMT measurements were averaged, and the adopted mean represented the overall CIMT. The carotid arterial walls were assessed for plaques, surfaces expressed as smooth, irregular, or ulcerated, and echogenicity classified as isoechoic, hypoechoic, hyperechoic, or calcified. Plaque mobility, location, and the number of affected arterial segments were also recorded.

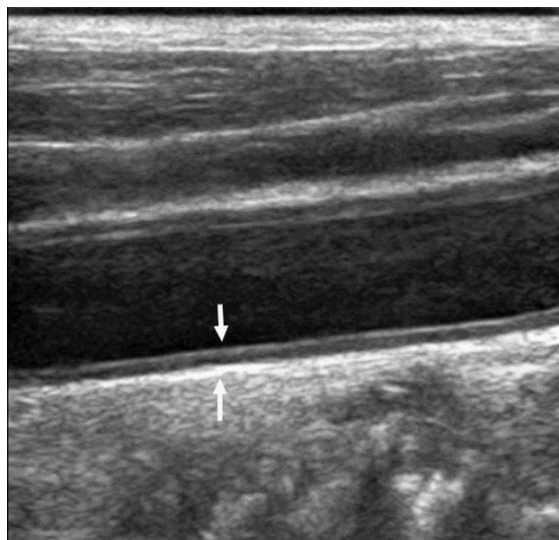


Figure 1: B-mode, the longitudinal US of the common carotid artery, shows the intima media thickness (IMT) between the white arrows.

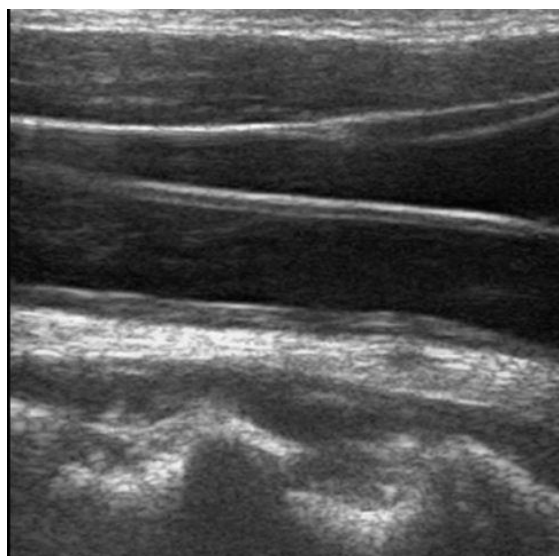


Figure 2: B-mode, longitudinal US of the common carotid artery showing the thickened intima media thickness (IMT).

Doppler imaging was done in longitudinal planes after optimised pulse repetition frequency. Sample volume gate of 2-3mm, colour velocity between 30-40cm/sec and a Doppler angle of 45-60° was maintained to reduce variation error. [19] Three spectral waveforms were measured by continuous-wave Doppler within one cardiac cycle in the mid-portion of the CCA and proximal ICA, 2cm beyond the CB. The highest and lowest velocities at systole and diastole were recorded as Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV), respectively. [19] The

spectral waveform in plaques and stenotic areas were measured at and distal to them, and in atrial fibrillation, the mean velocity of five consecutive beats was recorded. [19] Resistive index (RI) and Pulsatility Index (PI), dependent on blood velocity waveform shape and independent of the angle of insonation, were derived. [20] The PI is the difference between PSV and EDV divided by mean flow velocity, and RI is the difference between PSV and EDV divided by PSV. [21] The average scan time was 30 minutes per patient. After the procedure, the gel was wiped off the participant's skin with

soft tissue paper, and the neck returned to its normal position.

Data management and analysis

The generated data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows IBM version 23.0. Continuous and categorical variables were expressed as mean± standard deviation and proportions and frequencies (percentage), respectively. Values were compared for differences using the Student's t-test and Analysis of Variance (ANOVA). Pearson correlation coefficient (r) was used to assess the relationship between continuous variables, and statistical significance was defined as p< 0.05.

Results

The mean age of the study participants was 56.13 ± 6.93 years; they comprised 38% males and 62% females. The subjects' mean duration of HTN and DM diseases was 7.79 ± 8.97 years and 8.23 ± 7.04 years, respectively, while the mean age at diagnosis was 45.45 ± 11.48 years.

Among the subjects, DM was first diagnosed in 116 (58%), HTN in 72 (36%) and 12 (6%) were diagnosed with both DM and HTN at the same time. Two hundred and fifty-two (84%) and 288 (96%) of the participants did not consume alcohol or cigarettes. One (0.5%) subject and five (5%) controls were current alcohol consumers, while only one control was an active smoker. The socio-demographic parameters of study participants are shown in Table I.

Table I: Socio-demographic characteristics of the study participants

<i>Characteristics</i>	<i>Subjects n = 200</i>	<i>Controls n = 100</i>	<i>Chi-Square</i>	<i>P-value</i>
	n (%)	n (%)		
Age Group (Years)				
31-40	4 (2.0)	2 (2.0)	6.035	0.110
41-50	42 (21.0)	20 (20.0)		
51-60	96 (48.0)	57 (57.0)		
61-70	58 (29.0)	21 (21.0)		
Educational Qualification				
None	16 (8.0)	3 (3.0)	4.607	0.203
Primary	50 (25.0)	18 (18.0)		
Secondary	56 (28.0)	36 (36.0)		
Post-secondary	78 (39.0)	43 (43.0)		
Family History of Hypertension				
Yes	52 (26.0)	10 (10.0)	8.672	0.003
No	148 (74.0)	90 (90.0)		
Family History of Diabetes mellitus				
Yes	50 (25.0)	6 (6.0)	12.369	0.001
No	150 (75.0)	94 (94.0)		

The mean FBG of controls and subjects were 79.99 ± 13.07mg/dl and 125.93 ± 46.42mg/dl respectively with statistical significance (p =

0.001). The mean HbA1c among the subjects was 7.64 ± 4.47%; of this, good and poor glycaemic controls were observed in 72 (36%)

and 128 (64%), respectively. Deranged serum lipids were recorded in subjects and controls with statistical significance in the LDL-C ($p =$

0.002). The anthropometry and biochemical parameters of the study participants are shown in Table II.

Table II: Comparison of the anthropometric and biochemical characteristics of the participants

<i>Characteristics</i>	<i>Subjects n = 200</i>	<i>Controls n = 100</i>	<i>Chi-Square</i>	<i>P-value</i>
	n (%)	n (%)		
Body Mass Index				
Normal	52 (26.0)	41 (41.0)	5.522	0.063
Overweight	94 (47.0)	34 (34.0)		
Obesity	54 (27.0)	25 (25.0)		
Waist circumference				
Normal	16 (8.0)	37 (37.0)	25.749	<0.001
Overweight	74 (37.0)	32 (32.0)		
Obesity	110 (55.0)	31 (31.0)		
Total Cholesterol				
Normal	134 (67.0)	54 (54.0)	3.763	0.152
Intermediate	22 (11.0)	13 (13.0)		
High	44 (22.0)	33 (33.0)		
HDL-Cholesterol				
Normal	158 (79.0)	79 (79.0)	0.000	1.000
Abnormal	42 (21.0)	21 (21.0)		
LDL-Cholesterol				
Normal	128 (64.0)	42 (42.0)	9.715	0.002
Abnormal	72 (36.0)	58 (58.0)		
Triglyceride				
Normal	120 (60.0)	67 (67.0)	1.057	0.304
Abnormal	80 (40.0)	33 (33.0)		
Fasting Blood Glucose				
Normal	132 (68.0)	100 (100.0)	40.964	<0.000
Abnormal	64 (32.0)	0 (0.0)		
CIMT				
≥0.90mm	128 (64.0)	15 (15.0)	50.235	<0.000
<0.90mm	72 (36.0)	85 (85.0)		

HDL - High-Density Lipoprotein; LDL - Low-Density Lipoprotein; CIMT - Carotid Intima Media Thickness

The mean CIMT was significantly higher in the subjects ($1.00 \pm 0.3\text{mm}$) than the controls ($0.71 \pm 0.20\text{mm}$) ($p = 0.001$). The CB had the highest CIMT ($1.10 \pm 0.50\text{mm}$). The CIMT of CCA, CB and ICA were significantly higher among the subjects ($p = 0.001$ in each case). Higher CIMT was observed among the males and in the age

group 61–70 years; however, the observed differences were not statistically significant along the age and gender line ($p \geq 0.110$). Increased CIMT was observed in 64.0% and 15.0% of subjects and controls, respectively. It is distributed at the CCA, CB and ICA in 52%, 60.5%, 25.5% of subjects and 12.5%, 23%, 6.5%

of controls respectively. The CIMT had significant weak positive correlations with BMI ($r = 0.164, p = 0.020$) and WC ($r = 0.286, p = 0.001$) but weak negative correlation without significance with HbA1c ($r = -0.104, p = 0.304$).

A higher proportion of CP was seen among the subjects than controls (20% vs 2%; $p = 0.023$), with the highest distribution at the CB (70%). The prevalence of CP was higher among females than males (70% vs 30%) and on the left compared to the right side with significance (p

$= 0.023$ and 0.007 respectively). Unilateral CP was more frequent than bilateral CP (85.7% vs 14.3%). The prevalence of CP among the subjects increased with age with 10%, 35% and 55% recorded in the 5th, 6th and 7th decade respectively, whereas, in the controls, CP was noted in the 6th decade. The prevalence of CP among the subjects was significantly higher in those with abnormal BMI ($p = 0.033$) and abnormal WC ($p = 0.049$). The characteristics of the CP are represented in Table III.

Table III: Frequency, location and characteristics of carotid plaques in participants

Variables	Subjects n (%)	Controls n (%)
CP frequency	n = 40	n = 2
Right CP	18 (45.0)	1(50.0)
Left CP	22 (55.0)	1(50.0)
Right CP distribution	(n = 18)	(n = 1)
Distal CCA	4 (22.2)	0 (0.0)
Bulb	14 (77.8)	1 (100.0)
Proximal ICA	0 (0.0)	0 (0.0)
Left CP distribution	(n= 22)	(n = 1)
Distal CCA	8 (36.4)	0 (0.0)
Bulb	14 (63.6)	1 (100.0)
Proximal ICA	0 (0.0)	0 (0.0)
Right CP echotexture	(n = 18)	(n = 1)
Echolucent	0 (0.0)	0 (0.0)
Heterogenic	4 (22.2)	0 (0.0)
Echogenic	10 (55.6)	1 (100.0)
Calcified	4 (22.2)	0 (0.0)
Left CP echotexture	(n = 22)	(n = 1)
Echolucent	0 (0.0)	0 (0.0)
Heterogenic	0 (0.0)	1 (100.0)
Echogenic	18 (81.8)	0 (0.0)
Calcified	4 (18.2)	0 (0.0)
Right CP surface feature	(n = 18)	(n = 1)
Smooth	2 (11.1)	1 (100.0)
Ulcerated	2 (11.1)	0 (0.0)
Irregular	14 (77.8)	0 (0.0)
Left CP surface feature	(n =22)	(n = 1)
Smooth	14 (63.6)	1(100.0)
Irregular	8 (36.4)	0 (0.0)
Ulcerated	0 (0.0)	0 (0.0)

CP - Carotid plaque; CCA - Common Carotid Artery; ICA - Internal Carotid Artery

The subjects had lower mean PSV and EDV values with a statistically significant difference in the EDV ($p = 0.004$). These velocities were higher among males (PSV= $76.85 \pm$

11.87cm/sec ; EDV = $20.93 \pm 5.56\text{cm/s}$) than females (PSV = $76.26 \pm 19.04\text{cm/s}$; EDV = $20.88 \pm 5.87\text{cm/s}$), with no significant difference along gender line ($p = 0.11$). The PSV and EDV

values in the CCA, CB and ICA were higher on the left than the right in both the subjects and controls. However, positive moderate associations were observed on both sides among the subjects ($r = 0.444$) and controls ($r = 0.639$) with significant differences ($p = 0.026$ and 0.038). The subjects' average PI and RI were significantly higher ($p = 0.001$). Higher PI and RI values were observed among males but without statistical significance.

The comparison of the mean clinical, biochemical and ultrasound parameters of the participants are shown in Table IV. Significant

moderate positive correlations were observed between the PSV and EDV of the subjects ($r = 0.568$, $p = 0.0014$ and controls ($r = 0.480$, $p = 0.000$). Negative and weak associations were observed between the subjects' PSV and FBG and PSV and WC, BMI, SBP and DBP among the controls. The RI and PI had weak and moderate associations with PSV and EDV, respectively, with statistical significance ($p = 0.038$ and 0.0012 , respectively). The correlations between CIMT, PSV, EDV, PI, RI and cardiovascular risk factors are shown in Table V.

Table IV: Comparison of the mean values of selected clinical, biochemical, and carotid ultrasound parameters of the subjects and the controls

Variables	Subjects Mean \pm SD n=200	Controls Mean \pm SD n=100	t-test	P-value
Age (years)	56.12 \pm 7.34	56.15 \pm 6.55	-0.031	0.976
Height (m)	1.62 \pm 0.08	1.63 \pm 0.11	-0.443	0.658
BMI (kg/m ²)	28.01 \pm 4.70	27.13 \pm 6.11	1.138	0.257
WC (cm)	96.61 \pm 10.64	88.47 \pm 13.00	4.846	<0.001
FBG (mg/dl)	125.93 \pm 46.42	79.99 \pm 13.07	9.525	<0.001
LDL-C (mg/dl)	129.97 \pm 107.64	153.19 \pm 98.30	-1.593	0.113
HDL-C (mg/dl)	32.01 \pm 16.22	34.23 \pm 18.67	-0.896	0.371
Triglycerides (mg/dl)	120.77 \pm 60.91	105.93 \pm 48.05	1.913	0.057
TC (mg/dl)	188.85 \pm 114.39	205.99 \pm 98.18	-1.137	0.257
SBP (mmHg)	141.38 \pm 23.91	123.14 \pm 10.58	6.976	<0.001
DBP (mmHg)	83.94 \pm 13.58	79.67 \pm 7.90	2.718	0.007
CIMT (mm)	1.00 \pm 0.30	0.71 \pm 0.20	7.086	<0.001
PSV (cm/sec)	76.48 \pm 16.61	77.25 \pm 17.17	-0.321	0.748
EDV (cm/sec)	20.90 \pm 5.72	23.34 \pm 6.02	-2.934	0.004
PI	0.61 \pm 0.08	0.58 \pm 0.08	3.274	0.001
RI	0.72 \pm 0.06	0.69 \pm 0.07	3.441	0.001

WC - Waist Circumference; BMI - Body Mass Index; TC - Total Cholesterol; LDL-C - Low Density Lipoprotein Cholesterol; HDL-C - High Density Lipoprotein Cholesterol; CIMT - Carotid Intima Media Thickness; PSV - Peak Systolic Velocity; EDV - End Diastolic Velocity; PI - Pulsatility Index; RI - Resistance Index; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure; FBG - Fasting Blood Glucose.

Discussion

The remarkably higher CIMT observed in the present study is similar to the findings from various studies conducted among adults with hypertension and diabetes mellitus. [22-24] However, the mean CIMT among the subjects in the present study is higher than the values

reported in similar studies [22-25], indicating a higher CVD risk in the present cohort. Variations in the reported CIMT could be attributed to differences in sampling methods and size, geographic location and presence of a single disease compared to the two co-existing diseases in the present study. A positive correlation between CIMT and age among

subjects was similarly reported by some researchers, [24,26] suggesting an acceleration of the arterial intima media ageing process from

the synergistic effect of hyperglycaemia and elevated blood pressure. [23,24]

Table V: Correlation analyses between traditional cardiovascular risk factors and CIMT, PSV, EDV, PI and RI of participants

Variable	CIMT		PSV		EDV		PI		RI	
	r (p)	r (p)	r (p)	r (p)	r (p)	r (p)	r (p)	r (p)	r (p)	r (p)
	Subjects	Controls	Subjects	Controls	Subjects	Controls	Subjects	Controls	Subjects	Controls
Age (years)	0.151 (0.134)	0.081 (0.425)	-0.032 (0.752)	0.013 (0.898)	-0.012 (0.908)	0.051 (0.612)	-0.027 (0.792)	-0.026 (0.707)	-0.018 (0.856)	-0.046 (0.649)
FBG (mg/dl)	-0.046 (0.651)	0.199 (0.047)	-0.220 (0.028)	-0.014 (0.893)	-0.057 (0.571)	0.168 (0.096)	-0.125 (0.215)	-0.120 (0.235)	-0.216 (0.213)	-0.119 (0.239)
SBP (mmHg)	0.063 (0.531)	0.224 (0.025)	-0.148 (0.141)	-0.294 (0.003)	-0.200 (0.046)	-0.131 (0.193)	0.094 (0.351)	-0.084 (0.409)	0.084 (0.406)	-0.075 (0.460)
DBP (mmHg)	-0.032 (0.753)	0.057 (0.572)	-0.122 (0.228)	-0.292 (0.003)	-0.153 (0.129)	-0.105 (0.297)	0.084 (0.404)	-0.162 (0.107)	0.068 (0.503)	-0.141 (0.161)
WC (cm)	0.156 (0.121)	0.181(0.072)	0.036 (0.719)	-0.294 (0.003)	-0.118 (0.241)	-0.144 (0.154)	0.171 (0.089)	-0.095 (0.345)	0.176 (0.079)	-0.085 (0.402)
BMI (kg/m ²)	0.129 (0.201)	0.164 (0.103)	0.049 (0.629)	-0.340 (0.001)	-0.113 (0.263)	-0.147 (0.145)	0.192 (0.056)	-0.143 (0.157)	0.214 (0.033)	-0.120 (0.233)
HDL-C (mg/dl)	-0.165 (0.102)	- 0.173(0.085)	-0.076 (0.451)	-0.052 (0.605)	-0.296 (0.003)	0.026 (0.795)	0.285 (0.004)	-0.103 (0.308)	0.290 (0.003)	-0.119 (0.237)
LDL - C (mg/dl)	-0.215 (0.032)	-0.123 (0.224)	-0.054 (0.597)	-0.179 (0.075)	-0.041 (0.688)	-0.120 (0.234)	0.010 (0.918)	-0.019 (0.853)	0.022 (0.826)	-0.033 (0.748)
TC (mg/dl)	-0.222 (0.026)	-0.171 (0.090)	-0.058 (0.565)	-0.190 (0.058)	-0.041 (0.682)	-0.131 (0.195)	0.004 (0.969)	-0.017 (0.864)	0.024 (0.816)	-0.036 (0.724)
TG (mg/dl)	-0.017 (0.867)	0.179 (0.075)	0.087 (0.390)	-0.101 (0.317)	-0.127 (0.209)	-0.102 (0.314)	-0.064 (0.529)	0.047 (0.640)	-0.071 (0.480)	0.062 (0.537)
CIMT (mm)	-	-	-0.061 (0.544)	-0.091 (0.366)	0.052 (0.606)	0.204 (0.041)	-0.116 (0.250)	-0.287 (0.004)	-0.125 (0.214)	-0.268 (0.007)
PSV (cm/sec)	-0.061 (0.544)	-0.091 (0.366)	-	-	0.568 (>0.001)	0.480 (0.000)	0.222 (0.026)	0.343 (0.000)	0.207 (0.038)	0.268 (0.007)
EDV (cm/sec)	0.052 (0.606)	0.204(0.041)	0.568 (>0.001)	0.480 (0.000)	-	-	-0.663 (>0.001)	-0.635 (0.000)	-0.661 (>0.001)	- 0.637(0.000)
PI	-0.116 (0.250)	-0.287 (0.004)	0.222 (0.026)	0.343 (0.000)	-0.663 (>0.001)	-0.635 (0.000)	-	-	0.988 (>0.001)	0.972 (0.000)
RI	-0.125 (0.214)	-0.268 (0.007)	0.207 (0.038)	0.268 (0.007)	-0.661 (>0.001)	0.637(0.000)	0.988 (>0.001)	0.972 (0.000)	-	-

r - Correlation coefficient; p - Significance
 WC - Waist Circumference; BMI - Body Mass Index; TC - Total Cholesterol; LDL-C - Low-Density Lipoprotein Cholesterol; HDL-C - High-Density Lipoprotein Cholesterol; CIMT - Carotid Intima Media Thickness; PSV - Peak Systolic Velocity; EDV - End Diastolic Velocity; PI - Pulsatility Index; RI - Resistance Index; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure; FBG - Fasting Blood Glucose.

Although more female volunteers were in the present study, higher CIMT values were observed amongst the male participants. The additive effects of a female's hormonal protection on the CVS and resilience to hypertension before menopause may be contributory. [27] The present study revealed

that CIMT was equal bilaterally among the subjects. This did not agree with previous studies' reports, which documented higher CIMT on the left. [22,23,26] The direct origin of the left CCA from the aortic arch causes its higher hemodynamic change, resulting in increased wall thickness and a higher CIMT. [22,23,26] CIMT

was highest at the bulb among subjects, a finding similarly previously reported. [23]

The significant impact and positive correlation of CIMT with FBG and blood pressure among the subjects are consistent with other studies [24,28-29] despite differences in the methods of blood glucose and blood pressure measurements. The cumulative effects of hyperglycaemia and increased haemodynamic states on the vascular endothelium heighten the CIMT. [28-29] A non-significant difference and negative correlation observed between increased subjects' CIMT and HbA_{1c} agrees with the reports of Serdar *et al.* [26] and Okeahialam *et al.* [30] Atherosclerosis runs a chronic course, and HbA_{1c} reflects long-term glycaemic control, averaging blood glucose levels for the last two to three months. However, the difference reported between elevated HbA_{1c} and increased CIMT among Chinese and Japanese diabetic patients may be via insulin resistance, glucose excursion and advanced glycation of end products. [31-32] Significant positive correlation observed between increased CIMT and indices of visceral obesity (BMI and WC) among the subjects agrees with the reports by Okafor *et al.* [23] and Butt *et al.* [33] Visceral obesity causes the accumulation of macrophages in the adipose tissue and insulin resistance. [33] This, in turn, increases serum inflammatory cytokines and pro-inflammatory mediators, such as tumour necrosis factor- α (TNF), interleukin-6 (IL-6) and inducible nitric oxide synthase with resultant endothelial dysfunction, and ultimately endothelial atherosclerotic changes.[34] The prevalence of metabolic syndrome increases in obese individuals and substantially contributes to their atherosclerotic disease burden. [35] High concentrations of serum TG, TC, and LDL -C with reduced HDL-C, a vital component of metabolic syndrome, may heighten atherosclerosis risk.[36] In the present study, the prevalence of visceral obesity, hence, metabolic syndrome using the WC among the subjects (55%) and controls (31%) was high, as similarly reported by Unamba *et al.* [28] The present study

observed that subjects had better serum lipids than the controls, although, the difference did not achieve statistical significance. The use of statins in about three-quarters of the subjects combined with lifestyle modification could account for this. A significant but negative correlation observed between CIMT and serum lipids among the subjects is in discordance with the study of Okafor *et al.* [23], which reported a positive correlation among T2DM patients.

A higher incidence of carotid plaque noted in the older age group, and more on the left (55%) were also reported in other studies. [22-24] The direct origin of left CCA from the aorta facilitates plaque build-up in low wall shear stress areas.[37] Wall shear stress, generated by blood viscosity and blood flow velocity, makes arteries prone to atherosclerotic plaque development when they are low, especially in the carotid arteries of individuals at risk, increasing the incidence of stroke. [37-39] The hemodynamic disturbance at the carotid bifurcation increases endothelial cell damage, transient reversal of flow and separation with eddy formation, resulting in atherosclerotic plaques at the bulb. [38,40] Plaques at the bulb are a better predictor of coronary artery disease than those at the CCA. CP's presence is reportedly the strongest predictor for future cerebro-cardiovascular events. [41] A large proportion of the CP in the present study was echogenic. There was no echolucent or ulcerated CP as commonly seen in symptomatic individuals. [42]

Few studies investigated the relationship between carotid flow velocities and atherosclerosis. In this study, lower carotid flow velocity observed in the subjects was also reported among the hypertensives in some studies, accounting for their cardiac dysfunction and atherosclerosis. [43] Decreased PSV and EDV as well as increased PI and RI, reduce wall shear stress leading to endothelial dysfunction and reduced parenchymal blood flow with target organ damage. [44] EDV is associated with stroke development and

increases with vascular recanalisation or reperfusion.^[45] Resistive index, a close correlate with vascular resistance, is reportedly an independent predictor for CVD. ^[45] Strong correlations with statistical significances observed between EDV and PSV and between EDV and the derived flow velocities of the study participants could account for atherosclerosis as it increases vascular arterial resistance. In the present study, the relationships between carotid flow velocities and metabolic parameters (visceral obesity, dyslipidaemia, FBG) were significant, as observed in other studies.^[44] Hypertensive and diabetic patients have lower wall shear stress and lower blood flow velocity in their carotid arteries than healthy controls.^[45] An interplay among hyperglycaemia, hypertension, hyperlipidaemia with central and visceral obesity may contribute significantly to the development of reduced carotid blood flow velocity in the subjects. It could be one of the mechanisms by which metabolic syndrome and atherosclerotic plaque interact.

Conclusion

The marked structural wall changes, visceral obesity, dyslipidaemia with reduced carotid velocities observed in patients with co-existing hypertension and diabetes mellitus may be an early indicator for subclinical atherosclerotic changes, hence the CVD risk. Therefore, early detection of these vascular changes, especially the flow velocities, should be advocated. This will improve preventive and clinical care and attenuate their modifiable atherosclerotic risk factors.

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