Abstract

The intima media thickness (IMT) has been established as an early predictor of general arteriosclerosis in patients with hypertension. However, to date, there is paucity of information on IMT of common carotid artery in healthy patients and in patients with risk factors for cardiovascular diseases such as hypertension, diabetics and obesity in study area.

The aim of this study was to compare the carotid intima media thickness in patients with hypertension and normotensive adults attending Jos University Teaching Hospital Jos, Nigeria.

This prospective study was conducted over a period of four months (November 2012 to February 2013) on 200 hypertensive patients and 100 normotensive. The age range of the 300 patients comprising of 104 males and 196 females was 18 - 70 years with a mean age of 50.62 ± 10.46. The common carotid artery (CCA) was scanned using an ALOKA SSD-3500 ultrasound scanner with Doppler facility and a 7.5MHz linear transducer. Three measurements of the CIMT were obtained at 1cm proximal to the right and left carotid bulb and the mean value of the three measurements was recorded.

The overall mean CIMT was 0.89mm±0.13 and 0.61mm±0.10 for hypertensive and normotensive subjects respectively. Mean CIMT was significantly higher in hypertensive compared to normotensive subjects (p=0.000). CIMT correlated positively with age and blood pressure in hypertensives but had a negative correlation with BMI.

However in normotensives, CIMT correlated positively with age and BMI. Male hypertensives had higher CIMT when compared to female. In hypertensive subjects, overall right and left mean CIMT was 0.89 ± 0.13 and 0.89 ± 0.18, while in normotensives the overall right and left mean CIMT value was 0.61 ± 0.10 and 0.60 ± 0.10 respectively. There was no significant difference between the two sides. Artherosclerotic plaques were seen in the wall of the right CCA in six (3%) hypertensive patients, while none was seen in the normotensive group.

This study has shown that there is a significant difference in the CIMT of hypertensive compared to normotensive subject. Higher values of CIMT were seen in hypertensive subject compared to normotensive. Age, sex, BMI and blood pressure levels have significant effect on CIMT of hypertensive patients.

Keywords: Ultrasound; CIMT; hypertensive; normotensive.

Introduction

Hypertension is a chronic medical condition in which the systemic arterial blood pressure is elevated; greater than or equal to 140/90mmHg. It is the most common non-communicable cardiovascular problem worldwide afflicting humans. Approximately 15 to 37% of the world's adult population is afflicted\(^1\) and in Nigeria its prevalence is documented as 11.1%\(^2\). In more than 95% of hypertensive patients there is no specific underlying cause of hypertension and such patients are said to have essential/primary hypertension or idiopathic/unknown aetiology whereas only a small percentage have an identifiable cause (secondary hypertension).\(^3\)
Hypertension causes thickening of the intima media of large vessels with subsequent atheroma formation. Therefore hypertension is a risk factor for development of atherosclerosis, a systemic condition primarily affecting elastic arteries (carotid, aorta, and iliac arteries) as well as large and medium sized muscular arteries. Arterial wall modifications represent an early involvement of the target organs in patients with hypertension. Atherosclerotic plaques start developing in the carotid arteries and aorta simultaneously, actually preceding plaque occurrence in the coronary arteries.

Hypertension is one of the risk factors for stroke, myocardial infarction, heart failure, peripheral vascular disease and arterial aneurysm and a leading cause of chronic kidney disease. Assessment of subclinical and clinical target organ damage is a key element in the management of patients with hypertension. Practical and applicable examination for predicting the damage has been long-sought. One of such practical examination for predicting organ damage is the B-mode ultrasonic measurements of intima media thickness (IMT) in the carotid arteries. Other practical examination includes fundoscopy to check changes in the retinal and twenty-four-hour urinary excretion of protein and albumin. The B-mode ultrasound measurements of intima media thickness of the carotid arteries has been used extensively for evaluating the presence and progression of arteriosclerosis in patients with hypertension. Ultrasound measurements of IMT and plaque occurrence in the carotid arteries are important not only for the assessment of structural alterations but also because the extent of atherosclerosis in these vessels reflects the severity of arterial damage in other vascular territories.

High resolution B-mode Ultrasonography is a non-invasive, simple, safe, inexpensive, precise and reproducible method of examining and evaluating the walls of common carotid arteries for arterial wall thickening and atherosclerotic progression and regression. It also provides a measure of CIMT and detects presence of stenosis and plaques in patients with hypertension. This technique permits accurate quantification of the CIMT, which is generally considered as an early marker of atherosclerosis ultrasonographically. Thickening of intima-media complex also reflects generalized atherosclerosis and assessment of CIMT has been proposed as a noninvasive measure of cardiovascular disease burden in adults. Extra-cranial carotid arteries provide excellent and reproducible sites for IMT assessment because of their accessibility, adequatesize, and limited movement.

In this study B-mode ultrasound was used to compare the CIMT amongst hypertensive subjects and normotensive healthy volunteers.

**Materials and methods:**

This hospital based cross sectional study was carried out over a period of three months from November 2012 to February 2013 at Jos University Teaching Hospital Jos, Nigeria. Patients that fulfilled the inclusion criteria were recruited into the study. Patients were recruited based on the inclusion criteria until the targeted sample size was attained. The common carotid arteries of 300 subjects comprising of 200 hypertensive subjects and 100 normotensive subjects attending Jos University Teaching Hospital were scanned. The age range of the 300 patients comprising of 104 males and 196 females was 18–70 years with a mean age of 41.44 ±12. The inclusion criteria were: adult patients attending Cardiology clinic with confirmed primary hypertension, blood pressure ≥ 140/90 and aged 18-70 years; normotensive adults aged 18-70 years attending the general outpatient department. The exclusion criteria included: subjects below 18 years of age and above 70 years, patients with other associated cardiovascular risk factors such as diabetes, smoking and hypercholesterolemia, hypertensives on medication with blood pressure level < 140/90mmg, patients with diagnosed secondary hypertension (this information was
obtained from the patient's hospital record file), unwillingness to participate, pregnant women because of physiological changes and accompanying dilation of CCA and subjects in whom imaging circumstances were very poor, with limited boundary visualization of CCA or where there is anatomical constraint either a high carotid artery bifurcation or a short neck.

Approval to carry out the study was obtained from the ethical committee of the Jos University Teaching Hospital.

To ensure adequate compliance with inclusion and exclusion criteria, brief history was taken and general physical examination of the subjects was done. All patients had their fasting blood sugar level and fasting total cholesterol level checked in the chemical pathology laboratory and those with normal fasting blood sugar level between 2.5-5.5mmol and normal total cholesterol level between 3.5-6.5mmol were included in study. The blood pressure of the patients were measured by the same senior physician/Senior registrar in the cardiology clinic at presentation in a sitting position on the left arms using standard mercury sphygmomanometer (Accosson, cuff 12cm X 15cm) Hypertension was defined as blood pressure levels higher than or equal to 140/90 mmHg in at least two consecutive measurements. Hypertension was classified using W.H.O classification as Grade 1 hypertension (systolic blood pressure (SBP) 140-159mmHg, diastolic blood pressure (DBP) 90-99mmHg); Grade 2 hypertension (SBP 160-179mmHg, DBP 100-109mmHg) and Grade 3 hypertension (SBP≥180mmHg, DBP≥110mmHg). All normotensive subjects had their blood pressure checked at the General outpatient clinic and those with normal blood pressure ≤120/80mmHg were recruited for the study. The height (in meters) and weight (in kilograms) of each subject was taken using meter rule and Beam weighing scale respectively. The body mass index (BMI) was calculated as ratio of measured weight to square of the measured height (Kg/m^2). BMI was classified using WHO classification as underweight (BMI<18.5); Normal (BMI 18.5-24.9); Overweight (BMI 25.0-29.9); Obese (BMI≥30).

The examination of the CIMT was performed using the 7.5 MHz linear transducer ALOKA SSD-3500 ultrasound scanner equipped with Doppler facility. Patients were requested to remove jewelry around the neck. The B mode ultrasound of the CIMT were done with the subject lying supine to the right of the examiner with pillow support under the neck to achieve the desired neck extension and head turned 45° away from the side being scanned. Adequate amount of coupling gel was applied to the scan area to eliminate air gap between probe and skin surface. Right and left CCA were located by multiple longitudinal and transverse scans.

Three repeated measurements of CIMT were obtained in the longitudinal plane at the point of maximal thickness on the far wall of both CCA 1cm proximal to the carotid bulb, where it is clear of plaques. The position of the carotid bulb is defined as the point where the far wall deviated away from the parallel plane of the distal CCA (Figure 1). The IMT is the distance between the inner echogenic line representing the intima -blood interface and the outer echogenic line representing the adventitia-media junction (Figure 1). Measurements were repeated thrice on each side, unfreezing on each occasion and relocating the position of maximal IMT. The mean of the three measurements on each side was recorded. The overall mean was arrived at by averaging the mean of the right and left CIMT of hypertensive and normotensive subjects.

**STATISTICAL ANALYSIS**

The data obtained from the subjects was recorded in the questionnaire and was analyzed using Statistical Package for Social Sciences (SPSS) for windows version 19.0 (SPSS inc. Chicago, Illinois, USA). Mean ±standard deviation was used to summarize the variables. Comparison of mean and proportion was considered statistically significant if P value was equal to or less than 0.05. The results were presented in form of tables and figures.

**Results**

The mean age of subjects was 50.62 ± 10.46 years for both hypertensives and normotensives. There were 34.7% males and 65.3% females for both hypertensive and normotensive subjects. The predominant age group (Table 1) in both hypertensives and normotensive subjects was age group 51-60 years accounting for 57(28.5%) and 33 (33%) in hypertensive and normotensive subjects respectively. The overall mean CIMT for the hypertensive group in this study was 0.89 ± 0.13 and 0.62 ± 0.10 for the
The difference in CIMT is statistically significant (p=0.000). In hypertensive subjects, overall right and left mean CIMT was 0.89 ± 0.13 and 0.89 ± 0.18 respectively, while in normotensives the overall right and left mean CIMT value was 0.61 ± 0.10 and 0.62 ± 0.10 respectively. There was no statistically significant between the two sides in both hypertensives (p= 0.386) and normotensives (p=0.018).

The mean CIMT for male and female hypertensives were 0.92±0.16 and 0.87±0.12 respectively (p=0.11) and 0.62±0.09 and 0.61±0.09, (p= 0.70) amongst normotensive males and females respectively. Male CIMT values were higher than female CIMT value in both groups. However, gender difference in CIMT was not statistically significant in both hypertensives (P=0.11) and normotensives (P=0.70) (Table2).

In hypertensives, the mean CIMT for age group 21-30 and 61-70 was 0.70mm and 0.95mm respectively and in normotensives mean CIMT for age group 21-30 and 61-70 was 0.52mm and 0.83mm respectively (Table 3). The CIMT progressively increased with age in both hypertensives and normotensives. This increase was statistically significant (p=0.000) in both hypertensives and normotensives. (Table 3 and fig 3). The CIMT is higher in all age groups among hypertensives compared with corresponding normotensives. Age has a strong correlation with CIMT in both hypertensive and normotensive subjects (Pearson correlation =0.35 and 0.88 in hypertensives and normotensives respectively).

The mean BMI for the hypertensive group was 29.09±5.68 and 26.58± 6.17 for the normotensive group. The difference in BMI of subjects in both groups was statistically significant (p=0.001). The CIMT values in hypertensive subjects were significantly higher than in normotensive subject in each BMI grouping (p=0.000), (Table 4 and fig 4). However, BMI has a negative correlation with CIMT in hypertensives (Pearson correlation = -0.23) and positive correlation in normotensives (Pearson correlation= 0.22). These correlations were however not statistically significant (p=0.020) in hypertensive and (p=0.024) normotensives.

Carotid Plaques were seen in the CCA wall of six hypertensive patients (3%) in this study, while none was seen in the CCA of normotensive subjects. These plaques were more evident in the right CCA (Figures 5). These patients are scheduled to have ultrasound monitoring to assess future progression of the plaques.

**Table 1: Age distribution among Hypertensive and Normotensive subjects in Jan.**

<table>
<thead>
<tr>
<th>Age group (Years)</th>
<th>Hypertensive Frequency</th>
<th>Hypertensive Percent (%)</th>
<th>Normotensive Frequency</th>
<th>Normotensive Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 - 30</td>
<td>3</td>
<td>1.5</td>
<td>8</td>
<td>8.0</td>
</tr>
<tr>
<td>31 - 40</td>
<td>49</td>
<td>24.3</td>
<td>16</td>
<td>16.0</td>
</tr>
<tr>
<td>41 - 50</td>
<td>46</td>
<td>23.0</td>
<td>21</td>
<td>21.0</td>
</tr>
<tr>
<td>51 - 60</td>
<td>57</td>
<td>28.3</td>
<td>33</td>
<td>33.0</td>
</tr>
<tr>
<td>61 - 70</td>
<td>45</td>
<td>22.5</td>
<td>22</td>
<td>22.0</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

**Table 2: Mean CIMT of both hypertensive and normotensive subjects by gender.**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Hypertensive</th>
<th>Normotensive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Enq</td>
<td>RCIMT</td>
</tr>
<tr>
<td>Male</td>
<td>67</td>
<td>0.92</td>
</tr>
<tr>
<td>Female</td>
<td>133</td>
<td>0.86</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3: Mean CIMT value with age group in hypertensives and normotensives.**

<table>
<thead>
<tr>
<th>Age group (Years)</th>
<th>Hypertensives</th>
<th>Normotensives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCIMT</td>
<td>LCIIMT</td>
</tr>
<tr>
<td>21 – 30</td>
<td>0.67</td>
<td>0.73</td>
</tr>
<tr>
<td>31 – 40</td>
<td>0.51</td>
<td>0.54</td>
</tr>
<tr>
<td>41 – 50</td>
<td>0.63</td>
<td>0.67</td>
</tr>
<tr>
<td>51 – 60</td>
<td>0.96</td>
<td>0.93</td>
</tr>
<tr>
<td>61 – 70</td>
<td>0.99</td>
<td>0.92</td>
</tr>
</tbody>
</table>

P =0.000 across the age groups
Hypertension, a non-communicable disease is a common illness or disease in Sub-Saharan Africa as it is in most parts of the world. Therefore, adequate monitoring of cardiovascular risks cannot be overemphasized. This study has revealed the importance of noninvasive ultrasonographic investigation in the monitoring of hypertensive patients. Other studies had investigated CIMT in normal subject documenting baseline values of normal CIMT in their environment/geographic location. However, this study compared the IMT in hypertensive and normal cohort group and also correlated CIMT with age, sex, BMI and blood pressure levels.

The mean age of subjects was 50.62 ± 10.46 years for both hypertensives and normotensives subjects. Hypertension in the young is commonly due to a specific disease like renal and endocrine disease, known as secondary hypertension. In this study patients with secondary hypertension were excluded. There was also a female preponderance amongst hypertensive and normotensive subjects in this study.

The overall CIMT value was higher in hypertensive subjects than normotensives subjects (0.89mm Vs 0.61mm) and this difference was statistically significant. This is consistent with previous studies done. None of the reviewed previous studies had a contrary finding. These differences in the overall CIMT in the two cohort groups is presumably due to higher blood pressure levels in the hypertensive group. In hypertensive elevated blood pressure level can cause injury/damage to the endothelium of blood vessels with subsequent thickening of intima media complex via medial hypertrophy, a process specifically related to the disease. This thickening of the arterial wall is probably an adaptive mechanism to compensate for the persistent increase in blood pressure levels, and the thickening of the vessel wall have been demonstrated in vivo and vitro. This effect is not seen in normotensive subjects whose blood pressure levels are essentially normal, and thus normal CIMT is present in this group. Therefore increase in blood pressure has a significant effect on the intima media thickness.

In this study the overall mean CIMT of 0.89mm±0.13 in hypertensive subjects were higher compared to values from previous studies, Honzikova and Plavnik recorded 0.60 mm and 0.67mm respectively and Lemne in Sweden had an overall value of 0.73mm. On the contrary, the overall mean CIMT in normotensive subjects in this study was lower than 0.69mm obtained in study by

| Table 4: BMI with mean CIMT in both hypertensives and normotensives |
|-------------------|-------------------|-------------------|
| BMI               | Hypertensives     | Normotensives     |
|                   | (mm)             | (mm)             | (mm)             |
|                   | CIMT(mm)         | CIMT(mm)         | CIMT(mm)         |
| < 18.5            | 1 0.67 0.90 0.89 | 2 0.40 0.53 0.52 |
| 18.5 - 24.9       | 52 0.92 0.91 0.62 | 35 0.58 0.61 0.60 |
| 25.0 - 29.9       | 69 0.91 0.91 0.91 | 43 0.61 0.61 0.61 |
| ≥ 30              | 78 0.82 0.85 0.84 | 20 0.88 0.86 0.87 |
|                   | 200               | 100               |

P=0.000

![Graph showing relationship between age and CIMT in hypertensives and normotensives.](image1)

![Graph showing relationship between BMI and CIMT in hypertensives and normotensives.](image2)

Discussion

Hypertension, a non-communicable disease is a common illness or disease in Sub-Saharan Africa as it is in most parts of the world. Therefore, adequate monitoring of cardiovascular risks cannot be...
Lemme et al. but higher than 0.51 mm and 0.54 mm recorded by Honzikova and Plavnik respectively. The differences in CIMT observed in various studies in both hypertensives and normotensives could be due to sampling methods, sampling size, and racial differences. The sample size in this study was comparably larger than in other studies. Differences in life styles, diet and social habits, for instance high alcohol intake as well as chronic intake of potato chips in the study environment (Jos) is known to induce a pro-inflammatory state which is a risk factor for atherosclerosis and may be responsible for the differences in the CIMT observed in this study and other studies.

In this study, the method used at arriving at CIMT value involved taking three measurements 1 cm proximal to right and left carotid bulb and the mean value of the three measurements were recorded for each side; this was different from the method employed in some other studies. This method is simple, reliable, and reproducible. There is minimal inter and intra observer error. Using this method allows rapid identification of the target area and ensures that an identical area is assessed on follow-up. Certain infections such as viral hepatitis and human immunodeficiency virus infection have been shown to be associated with increased CIMT probably due to presence of pro-inflammatory cells which are risk factor in artherogenesis.

Bilaterally, there was a noticeably higher right and left CIMT value in hypertensives compared to normotensives (0.89±0.13 mm and 0.61±0.10 mm in right and left respectively). Many other studies shows similar trend, Sharma recorded 0.968 mm and 0.969 mm vs 0.551 and 0.555 mm; Adaikkappan recorded 1.01 mm and 1.09 mm vs 0.74 mm and 0.72 mm; Umeh recorded 0.751 mm±0.129 and 0.756 mm±0.130 vs 0.670 mm±0.107 and 0.638 mm±0.088; Okeahialam recorded 93 mm±0.21 and 93 mm±0.15 vs 0.91 mm±0.17 and 0.91 mm±0.13; Planvnik recorded 0.67 mm±0.13 and 0.62±0.09 vs 0.54 mm±0.09 and 0.52 mm±0.11 for hypertensives and normotensives respectively.

The mean CIMT value in the left CCA was higher than the right CCA (0.62 mm±0.10 vs 0.61 mm±0.10) in normotensive group of patients studied. Although, this findings was not statistically significant (P=0.18). This result was consistent with the study by Sharma but contrary to findings in other studies. There was no difference in the measured CIMT value between the left and right CCA in hypertensive group (0.89±0.13 Vs 0.89±0.13) and this finding is similar to those in a study in Jos by Okeahialam. However some other studies showed a difference in values between the measured left and right CIMT with the left CIMT value higher than right. While another study showed right CIMT value to be higher than the left. In this study, equal value of CIMT observed on both CCA for hypertensive and the higher value of CIMT recorded in the left CCA in normotensive, are contrary to the findings of Lemme who recorded higher CIMT value in the right CCA for both hypertensive and normotensive subjects. The reason for such differences between IMT of right and left common carotid artery sides are unknown. However, the left common carotid is a direct branch of the aorta while right common carotid results from division of brachiocephalic trunk. Therefore it is possible that dissimilarities have existed in the arterial growth between both arteries and/or that flow mediated mechanical forces applied to carotid wall differ between the two sides.

The mean CIMT value of male and female hypertensives were higher than the mean CIMT value of male and female normotensive (male and female hypertensives CIMT values were 0.92 mm vs 0.87 mm, while in normotensive males and females CIMT value were 0.62 mm vs 0.61 mm. In both groups males have a higher CIMT value than females. This relationship was not statistically significant (Hypertensive P=0.11 and Normotensive P=0.70). This finding was consistent with other studies and may be explained by the sex variation in the development of artherogenesis. Males have a higher chance of developing artherosclerosis more often than females, although the reasons are not known but may be due to the fact that males are more prone to psychological and environmental stress than females.

There was progressive increase in CIMT from age 18 years to 70 years in hypertensive and normotensive groups of patients. The CIMT values in hypertensive subjects were higher than CIMT value of normotensive subjects in each age group. Most of the studies reviewed also consistently showed with increased CIMT with age. This study also showed that age has a strong
correlation with CIMT values recorded in both hypertensive and normotensive subjects investigated (Pearson correlation 0.35 and 0.88 in hypertensives and normotensives respectively). The increase in mean CIMT with age in normotensive subjects 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. In hypertensives, higher CIMT value with age could probably be due to the combined effect of increase blood pressure levels and aging process on the intima media. Also the impact of blood pressure levels on the intima media has been considered as an accelerated form of aging and hypertensive patients develop aging process in their arterial walls earlier in life than normotensives. There was also progressive increase in mean CIMT with BMI in normotensive subjects. This was statistically significant. Mean CIMT correlated positively with BMI in normotensive but negatively in hypertensive subjects. Similar finding was demonstrated in the studies by Honzikova and Planvik. BMI has been shown to influence the CIMT but the role of BMI in arterial wall thickening is poorly understood and its influence is probably independent of age.

A plaque is defined as a focal structure arising from the intima media layer of the arterial wall and encroaching into the arterial lumen. Plaques are sometimes found in the wall of the vessel of hypertensive patients. Carotid Plaques were seen in the vascular wall of six hypertensive patients (3%) in this study, while none was noted in the CCA of normotensive subjects. These plaques were more evident in right CCA. This finding is similar to what was recorded by Lemne study where they also recorded higher number of plaques in hypertensives which were also evident in the right carotid arteries. Umeh in Ibadan also recorded a higher number of plaques among hypertensive subjects.

**Limitation:** The limitations encountered during this study included that some sizes and contours of the neck posed difficulty in examination, presence of calcium deposits in the wall of the carotid artery made it difficult to evaluate the thickness of the intima media and the end segment of the carotid artery in some patients was not clearly depicted by ultrasound. However these subjects were excluded from the study.

**Conclusion:** This study has shown that there is a significant difference in the CIMT of hypertensive compared to normotensive subject. Higher values of CIMT were seen in hypertensive subject compared to normotensive. Age, sex, BMI and blood pressure levels have significant effect on CIMT of hypertensive patients. B-mode ultrasound is a reliable, readily available, cheap and noninvasive imaging modality that is useful in the management of hypertension.

**Recommendation:** It is recommended that all hypertensive patients should have routine carotid artery USS for CIMT measurement. Noninvasive B-mode ultrasound should be used as basic predictive investigation for CIMT and government health promotional activities should include routine check of CIMT in hypertensive patients.

**References:**

11. Allan PL, Mowbray PI, Lee AJ, Fowkes FG. Relationship between carotid intima-media thickness and symptomatic and asymptomatic peripheral arterial disease: The Edinburgh Artery Study. Stroke 1997;28:348-353. 
19. Gariepy J, Massonneau M, Levenson J, Heudes D, Simon A. Evidence for in vivo...


