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Carotid intima media thickness evaluation by ultrasound comparison amongst healthy, diabetic and hypertensive Pakistani patients

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Abstract

Objective: To compare carotid Intima media thickness and atherosclerosis burden amongst healthy, diabetic and hypertensive Pakistani patients.

Methods: A cross-sectional study was carried out at the Department of radiology and family medicine, Aga Khan University Hospital Karachi from April 2014 to July 2015. Bilateral carotid ultrasound was done in 133 healthy adults, 65 hypertensive, 31 type-2 diabetic and 37 hypertensive with type-2 diabetes patients. Normal adults were matched for age and gender. Mean intimal media thickness was measured for common and internal carotid arteries. Presence or absence of atherosclerotic plaque was also identified. Height, weight, ethnicity, socioeconomic status and other risk factors were also assessed. Ultrasound findings were compared between healthy and diseased patients through statistical tests.

Results: A total of 266 patients participated (Controls=133, Hypertensive=65, Diabetic=31, and Diabetes with Hypertension=37). There was no significant difference in the baseline characteristics between the four patients' groups for age ($p>0.05$) and gender ($p>0.05$).

The mean carotid intima media thickness of right common carotid artery was significantly higher in patients with diabetes along with hypertension as compared to the control group ($p=0.03$). For (RICA) Right Internal Carotid Artery, (LCCA) Left Common Carotid Artery and (LICA) Left Internal Carotid Artery, there was a significantly higher thickness among patients with hypertension as compared to the control group with $p=0.011$, $p=0.002$, and $p=0.039$ respectively.

Conclusion: Increased CIMT is most likely associated with underlying chronic diseases. Ultrasound is a non-invasive, easily available and useful modality for early detection and prevention of vascular atherosclerosis.

Keywords: Carotid Intima media thickness, Ultrasound, Hypertension. (JPMA 66: 1396; 2016)

Introduction

Chronic diseases (CD) which include Cardiovascular disease (CVD), hypertension (HTN), Diabetes mellitus (DM) and Chronic kidney disease (CKD) are a major worldwide health problem.^{1,2} They are major health concerns for developing countries with gradually increasing trend requiring sustained research.³ Amongst all CD, Hypertension alone is a leading cause of death from cardiovascular atherosclerotic disease. According to National health survey of Pakistan (1990-94), HTN affects 18% of adults and 33% of middle age adults (age of 45 years and above). The prevalence of DM in Pakistan is also high ranging from 7.6-11%.^{4,5} Previous studies have demonstrated that diabetic patients have greater chance of morbidity and mortality associated with cardiovascular disease and three out of four die because of cardiovascular complications.^{6,7} The exact data regarding presence of CKD in our population is missing; however, approximately 15-20% persons, 40 years of age or above

have reduced glomerular filtration rate as a measure of CKD.⁸ CKD patients are at a greater risk of cardiovascular diseases due to rapid atherosclerosis.^{9,10}

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.^{11,12} CIMT is highly associated with cardiovascular risk factors¹³ and robust predictor of cardiovascular outcomes and cerebrovascular complications.¹⁴ The measurement of CIMT has also been advocated and proposed as a non-invasive tool for cardiovascular risk assessment in primary prevention.¹⁵ Ultrasound especially B-Mode ultrasound is the modality of choice for CIMT evaluation as it is accurate, safe, cost-effective and easily available. According to American Heart Association guidelines, Carotid ultrasound is useful for detection of carotid artery disease in symptomatic patients but it is not recommended in asymptomatic patients without having any risk factor for vascular atherosclerosis.¹⁶ Our previous study¹⁷ has also shown effectiveness of pre-operative carotid ultrasound for carotid artery disease assessment in patients undergoing coronary artery bypass graft surgery to reduce

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cardiovascular complications.

CIMT data related to high risk south Asian population is limited and to the best of our knowledge no research has been done in our Pakistani population on carotid Intima-media thickness for cardiovascular risk assessment in hypertensive and diabetic patients. Our hypothesis was that hypertensive and diabetic patients will be having more CIMT as compare to normal participants. Therefore the primary objective of this study was to estimate the carotid intima media thickness with pre- clinical atherosclerosis in Hypertensive and Diabetic patients and compare it with non-hypertensive, non-diabetic, normal control group.

Patients and Methods

This study was approved by hospital ethics committee and informed written consent was taken from all participants. Ultrasounds were done free of cost at radiology department and participants were recruited from family medicine clinic at Aga Khan University Hospital Karachi, Pakistan. Inclusion criteria were all adult patients presenting to the family medicine clinic having Pakistani ethnicity with diabetes, and hypertension, healthy individuals were selected for the control group. Controls were matched as much as possible for age and gender with cases. Patients having known carotid artery disease or past endarterectomy were excluded. The subjects were invited to participate in this study when they presented to family medicine clinic. After obtaining written informed consent, patient's demographics and relevant history was taken by a trained data collector in the clinic and patient was informed about the ultrasound examination. Participant was labeled as control [Group-A] when there was no history of HTN and no high blood pressure (more than 150/100 mmHg) on two repeated measurements, no angina according to WHO Rose angina questionnaire,¹⁸ no stroke as assessed by QVSFS,¹⁹ no history of DM, CKD, lipid disorder or medication intake. Ultrasound was done by a single qualified radiologist having more than ten years experience in vascular Sonography by using 6-10 MHz linear probe who was blinded to clinical status of participants. Ultrasound was done with Study participant in a supine position with extended neck and arms on both sides. Ultrasound measurements were

done in a standardized way by using electronic caliper installed in ultrasound machine with angle of insonation less than 60 degrees. CIMT was defined as distance between the leading edge of luminal echo to leading edge of the adventitia of the media. During periods of diastole, the image was frozen and the measurements were assessed 1cm proximal and distal to carotid bulb on both sides away from atherosclerotic plaque. Image documentation was done by taking hard print as well as sending on PACS. Mean intima media thickness was measured by taking three set of measurements in each artery on either side. Presence or absence of atherosclerotic plaque (focal thickening with or without calcifications) or significant carotid stenosis (more than 50% morphological luminal narrowing) was also assessed (The detail data of the study participants are shown in the Figure). Carotid ultrasound findings were documented in patient's medical record and formal report was given to patient for patient's future management. The clinical management was determined by the primary physician.

Data was entered in Excel and analysis was performed in SPSS version19. Descriptive and analytical statistics including ANOVA was calculated; p-value less than 0.05 was considered as significant.

Results

A total of 266 patients were included in the study (Controls=133, Hypertensive=65, Diabetic=31, and Diabetes with Hypertension=37). Overall, there was a higher proportion of female patients 63.9% (n=170) in our data set. There was no significant difference in the baseline characteristics of patients between the four

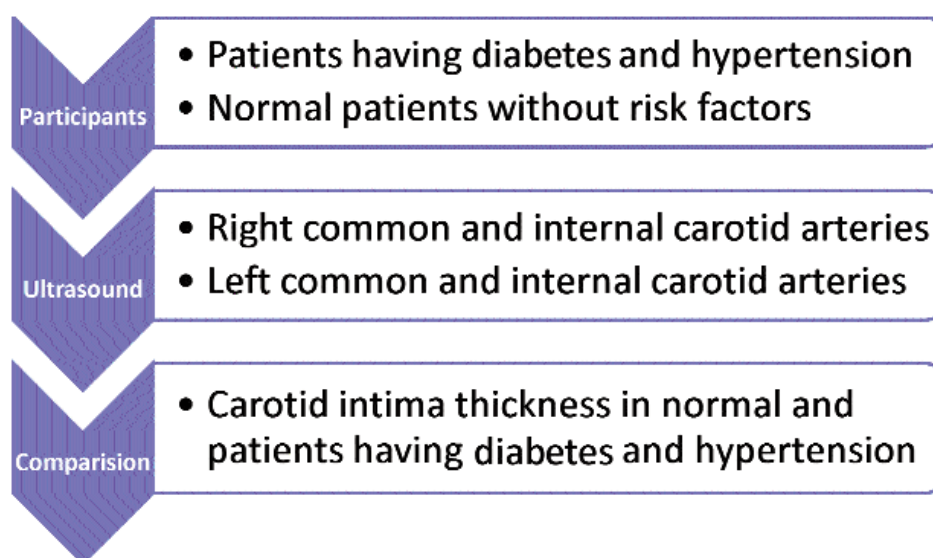


Figure: Flow diagram of study participants.

Table-1: Baseline comparison of Control, Hypertensive, Diabetic and Diabetic and Hypertension groups.

Variables value	Control Group (n=133)		Hypertensive patients (n=65)		Diabetic patients (n=31)		Patients with Diabetes and Hypertension (n=37)		F- statistics	P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Age	54.80	8.708	54.60	8.558	53.84	10.007	56.62	7.872	0.664	0.575
Gender										
Male n(%)	48	36.1%	17	26.2%	16	51.6%	15	40.5%	6.339	0.096
Female n(%)	85	63.9%	48	73.8%	15	48.4%	22	59.5%		
BMI	26.47	3.701	27.41	4.591	26.93	3.950	28.88	3.916	3.710	0.012*

*Significant difference was found between control group and HTN+DM group on posthoc Dunnett t (2-sided) test

**Chi square test for trend.

Table-2: Comparison of RCCA, RICA, LCCA and LICA intimal thickness among the four study groups.

Variables value	Control Group (n=133)		Hypertensive patients (n=65)		Diabetic patients (n=31)		Patients with Diabetes and Hypertension (n=37)		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F- statistics	P
RCCA	0.543	0.104	0.579	0.135	0.569	0.167	0.613	0.176	3.085	0.028*
RICA	0.501	0.093	0.554	0.144	0.553	0.116	0.557	0.201	3.797	0.011**
LCCA	0.550	0.120	0.626	0.171	0.546	0.148	0.609	0.170	5.011	0.002**
LICA	0.498	0.092	0.546	0.171	0.503	0.110	0.545	0.159	2.838	0.039**

*Significant difference was found between control group and HTN+DM group on posthoc Dunnett t test

**Significant difference was found between control group and HTN group on posthoc Dunnett t test

RCCA: Right Common Carotid Artery thickness in mm; RICA: Right Internal Carotid Artery thickness in mm

LCCA: Left Common Carotid Artery thickness in mm; LICA: Left Internal Carotid Artery thickness in mm

SD: Standard Deviation.

groups for age ($p > 0.05$) and gender ($p > 0.05$) [Table-1]. However, there was a significant difference between control group and patients with Diabetes and Hypertension in terms of baseline BMI [mean = 26.47 ± 3.701 versus mean = 28.88 ± 3.916 ; F-statistics=3.7; $P=0.012$].

Since normal cutoff value of IMT is not known in our population, therefore mean intima thickness (0.52 ± 0.027 mm) of control patient was taken as reference value. The overall prevalence of abnormal intima thickness (>0.52 mm) was 73% ($n=97$) in our sample. The prevalence was 77% ($n=50$) among hypertensive group, 61% ($n=19$) among diabetic group, 76% among patients with both hypertension and diabetes ($n=28$) and 70% ($n=93$) in the control group. The prevalence of atherosclerotic plaque was identified on ultrasound was 0.7% in controls ($n=1$) and 6.8% in all cases combined ($n=9$).

Table-2 shows the comparison of intimal thickness of right common carotid artery (RCCA), right internal carotid artery (RICA), left common carotid artery and left internal carotid artery between control group, hypertensive, patients with diabetes and patients with both diabetes and hypertension [Table-2].

There was a statistically significant difference of mean intimal thickness of RCCA between the control group and patients with diabetes and hypertension (mean = 0.543 ± 0.104 mm versus mean = 0.613 ± 0.176 mm; $p=0.028$). The tendency of increased intimal thickness was higher among patients with diabetes along with hypertension whilst there was no difference between other groups as determined by posthoc test. On the other hand, the mean thickness of RICA was only significantly different between hypertensive group and the control group (mean = 0.501 ± 0.093 mm versus mean = 0.554 ± 0.144 mm; $p=0.011$). Similarly, the mean thickness of LCCA and LICA were also significantly higher in hypertensive group as compared to the control group (mean = 0.55 ± 0.12 mm versus mean = 0.626 ± 0.171 mm; $p=0.002$) and (mean = 0.498 ± 0.092 mm versus mean = 0.546 ± 0.171 mm; $p=0.039$) respectively. No difference was found between the intimal thickness of patients with diabetes and patients with hypertension along with diabetes.

Discussion

This preliminary study can be used as an eye-opener to take quick initiatives for the prevention and early detection

of cardiovascular diseases. It is known that South Asian population is at significantly higher risk of coronary artery disease and other cardiovascular problems.²⁰ The high prevalence of abnormal CIMT in our study points towards the need for additional measures for early detection of the problem in South Asian population. This study has shown that the risks of cardiovascular disease might be detected early as a result of using CIMT screening through ultrasound. Other studies have also readily pointed out the importance of CIMT screening in primary prevention.¹⁵

Patients with hypertension and hypertension with diabetes had the highest average CIMT found in our study which is consistent with the fact that hypertension has the greatest effect on IMT through medial hypertrophy.²¹ In addition, diabetes also leads to increase risk of atherosclerosis by increasing intimal thickness.²² However, studies have shown that hypoglycaemic drugs may help in decreasing intimal thickness.^{23,24} Thus, early detection of abnormal CIMT might be very helpful in reversing the process through medication and other life style interventions. Reduction in CIMT may also decrease the incidence of brain infarction as abnormally high intimal thickness is also associated with increased risk of brain infarction. The mean CIMT of our control was 0.52mm which is lower than the published studies,²⁵ highlighting the importance of defining the cutoff value of normal CIMT and percentiles in south Asian population for flawless interpretations.

There were some limitations in this study. First, the study was conducted in a hospital setting which might have resulted in showing higher prevalence of abnormal CIMT as compared to the general population. A large scale population-based study would estimate more accurate prevalence of abnormal CIMT. Second, although most of the baseline characteristics were matched between the study groups, BMI was significantly different among the selected groups. This was an inherent problem expected in the study as patients with diabetes and hypertension were expected to have higher BMI than healthy individuals. However, this was even more worrisome finding that the study revealed high prevalence of abnormal CIMT even in relatively non-obese, health participants with a significantly lower BMI.

The future research should focus on determining the actual relationship of cardiovascular disease with each unit increase in intimal thickness in Pakistani population. Moreover, there is no data available on cut off values of intimal thickness for Pakistani population. Therefore, future studies should also focus on developing the normal range for Pakistani population which may pertain to other

South Asian population in the region.

Conclusion

The prevalence of abnormal CIMT is unacceptably high in our population not only in hypertensive and diabetic patients but also among patients without any cardiovascular disease. In addition to the routine screening measures, carotid ultrasound should be integrated as a mandatory screen procedure for patients with chronic hypertension, diabetes, and for those patients who are expected to be at higher risk due to unhealthy diet based on dietary assessments. This early screening could identify patients at risk at an early stage and aggressive changes in life style and dietary habits can reduce or possibly reserve the progression towards cardiovascular problems.

Disclosure: No.

Conflict of Interest: No.

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