Original Article

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Carotid Artery Intimal Medial thickness in Diabetic and Non-Diabetic Subjects in Central Kerala

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Abstract

Background: Increase in intimal medial thickness (IMT) of the carotid arteries is contemplated as a guide to atherosclerotic vascular disease and subclinical organ damage and foretell cardiovascular disease. The study aimed to analyse IMT in non-diabetic and diabetic subjects. **Subjects and Methods**: There were 105 diabetic and 95 non-diabetic subjects in this study. Common carotid artery (CCA) IMT was calculated using a linear probe of a high-resolution ultrasound medical system. **Results**: Diabetic subjects (0.95 mm) showed significantly higher mean intimal medial thickness (IMT) when compared non-diabetic subjects (0.85 mm) ($p < 0.05$)**.** Correlation of IMT was seen with age, total cholesterol, triglycerides, HDL & LDL cholesterol and systolic blood pressure (SBP) in diabetic subjects. Total cholesterol, SBP and diastolic blood pressure (DBP) showed a correlation with IMT in the non-diabetic subjects. Age, total cholesterol, SBP, and diabetes were independent risk factors for intimal medial thickness in multivariate linear regression analysis. **Conclusion**: Higher intimal medial thickness was seen in diabetic subjects when compared to non-diabetic subjects. We conclude that age, total cholesterol, SBP and duration of diabetes showed a significant correlation with IMT. IMT can be considered as a screening tool in diabetic patients for the early detection of atherosclerosis.

Keywords: Diabetes Mellitus, Ultrasonography, Atherosclerosis.

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Introduction

The intima-media thickness (IMT) is equivalent to the intima-media complex, which includes smooth muscle, connective tissue and endothelial cells, the area of fat deposition in atherosclerosis. Carotid IMT (CIMT) is used as a non-invasive and surrogate measure of atherosclerosis.[1–9] Good correlation of subsequent progress to myocardial infarction and stroke with IMT measurements is seen.[10,11] Studies have shown that for each 0.1-mm rise in carotid IMT, the relative risk of cardiovascular disease rises by 15% and that of cerebrovascular disease by 18%.[12] CIMT also correlates with clinically established cardiovascular disease and the Framingham Score.[13–17] In type 2 diabetic patients' duration of diabetes, hypertension, hyperglycemia, dyslipidemia, and smoking have been identified as significant risk factors for stroke.[18] Further IMT measurement is non-invasive, inexpensive, and easily available and carries no risk for the patient. A high prevalence of premature coronary artery disease and diabetes is seen in Asian Indians.[19–23] India is among the leaders in a number of diabetic patients in the world.[24] Diabetes leads to atherosclerotic vascular disease and complications like coronary artery disease (CAD) and stroke. This study looks into IMT in diabetic and non-diabetic subjects in central Kerala.

Subjects and Methods

This is a cross-sectional study that included 200 participants. The criteria used for the diagnosis of diabetes were fasting blood sugar (FBS) higher than $\geq$126 mg%, a postprandial blood sugar (PPBS) higher than $\geq$200mg% and random plasma glucose $\geq$200mg%. Non-diabetics were those who had a normal FBS test and none of the items above. The present work was undertaken in collaboration between the Department of Radiology and Medicine, SNIMS, Chalakka, during the period May 2017 to May 2020. After approval by the ethical committee, due consents were taken from the respective patients and guardians of the patients. Subjects were selected from inpatient and outpatient clinics of the medicine department. A thorough medical history and complete physical examination of all patients were done followed by investiga-

Table 1: Comparison of IMT based on diabetic status

Diabetic status	Mean	SD	N	T	P
Non-diabetic	0.085	0.024	105	2.97	0.003
Diabetic	0.095	0.023	95		

tions including, FBS, PPBS, lipid profile and ultrasonography for CIMT measurement.

Intimal medial thickness assessment

The IMT thickness of the carotid arteries was calculated using a high-resolution ultrasonography machine (Philips Affiniti 50) having a linear array transducer and a frequency range of 7- 15 MHz. Patients were positioned with the head slightly extended and turned towards the opposite side of the carotids being assessed. To assess CIMT, far-wall IMT measurements were taken, because they are viewed as more accurate than near-wall measurements. The measurement is made between the two bright lines made by blood-intima interface and media-adventitia junction as the far and near-wall respectively. CIMT of both sides was assessed at 3 sites (point of maximum thickness, and at sites 1 cm proximal and distal to it and free from plaques) on the sagittal plane. The mean CIMT was defined as the mean IMT of the right and left common carotid arteries, calculated from 3 readings on both sides. All measurements were assessed by experienced radiologists who were blinded to the diabetic status of the subjects.

Statistical analysis

The Independent t-test was used to compare quantitative parameters between categories. A Chi-square test was used to the association between categorical variables. Karl Pearson Correlation Coefficient was used to find our relationship of IMT with age, serum cholesterol, serum triglycerides, HDL cholesterol, SBP and DBP as independent variables. Multiple linear regressions were done to find the independent influence of selected variables on IMT. For every statistical analysis, $p<0.05$ was taken as the point for statistical significance. Statistical analyses were done using statistical software, IBM SPSS version 20.0

Results

Mean CIMT in the non-diabetic group was 0.85 mm and in the diabetic group was 0.95 mm**.** The range of CIMT values in non-diabetics was 0.4 - 1.7 mm and in diabetics, 0.4- 1.85 mm.

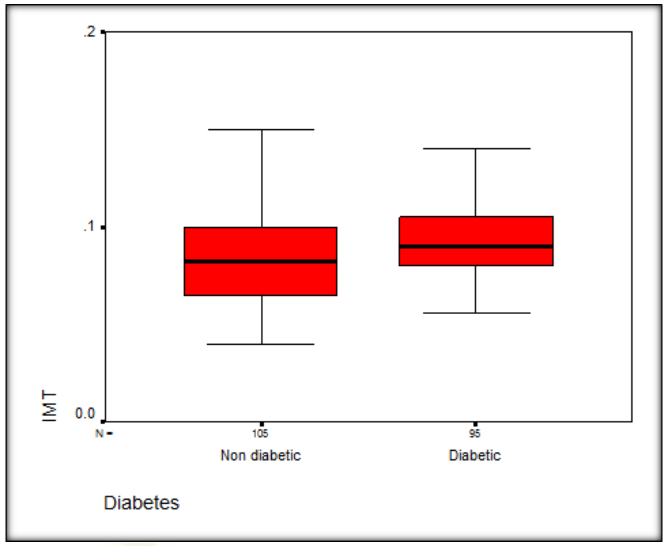

Figure 1: Box plot for CIMT based on diabetic status

The diabetic group had higher total cholesterol, triglycerides, HDL and LDL than non-diabetic subjects but only total cholesterol showing a significant difference

Increased CIMT was seen in the diabetic group compared with a non-diabetic group in both gender in our study, but only the non-diabetic group showing a significant difference.

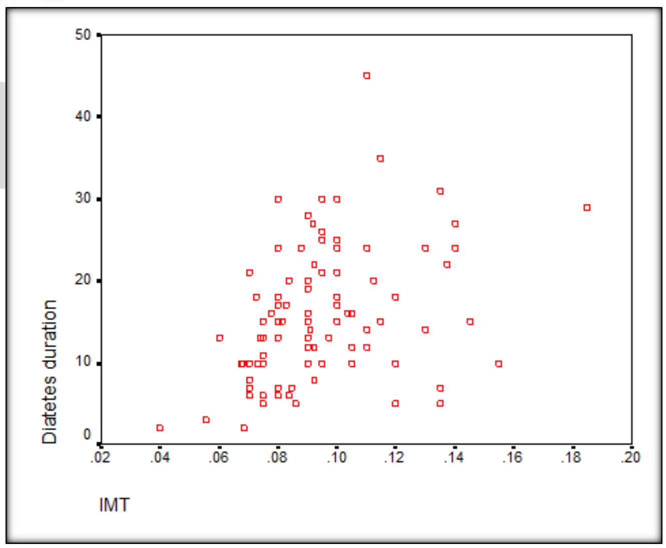

Figure 2: Scatter diagram for diabetes and CIMT (r = 0.366, p<0.01)

In the non-diabetic group cholesterol, SBP and DBP showed a positive correlation with IMT whereas, in the diabetic group, age, cholesterol, triglycerides, LDL and HDL cholesterol,

Table 2: Comparison of lipid profile based on diabetic status

	Non-diabetic			Diabetic			T	P
	Mean	SD	N	Mean	SD	N		
CHO	195.4	37.6	105	205.7	34.9	95	2	0.047
TRI	142.6	39.1	105	148.8	32.9	95	1.2	0.230
HDL	35.4	8.8	105	37.1	5.7	95	1.56	0.120
LDL	125.9	28.8	105	129.2	27.4	95	0.82	0.412

Table 3: Comparison of CIMT with sex among diabetic and non-diabetic patients

Diabetes	Sex	Mean	SD	N	T	P
Non-diabetic	Male	0.091	0.025	47	2.31	0.023
	Female	0.080	0.021	58		
Diabetic	Male	0.097	0.021	48	1.05	0.299
	Female	0.092	0.025	47		

Table 4: Correlation of CIMT with lipid profile, blood pressure and age among diabetic and non-diabetic patients

	Diabetic		Non-diabetic	
	R	p	r	P
CHO	0.522	p<0.01	0.314	0.002
TRI	0.407	p<0.01	0.134	0.195
HDL	-0.411	p<0.01	-0.134	0.196
LDL	0.471	p<0.01	0.152	0.142
Age	0.43	p<0.01	0.191	0.063
SBP	0.319	0.001	0.409	p<0.01
DBP	0.035	0.723	0.326	0.001

SBP, and duration of diabetes showed a positive correlation with CIMT

The mean CIMT of the non-diabetic group in normotensive and hypertension subjects was 0.73 mm and 0.90 mm, respectively. In the diabetic group, normotensive and hypertension subjects had the mean CIMT values of 0.85 mm and 0.98 mm respectively

Multivariate linear regression analysis was done including details of both diabetic and non-diabetic groups and counting diabetes as an independent variable. Age cholesterol, HDL cholesterol, SBP and diabetes exhibited an association with IMT

Discussion

CIMT is regarded to be a non-invasive marker of atherosclerotic vascular disease,[1–3] coronary artery disease and recurrent ischemic stroke.[25–29] The earliest indication of atherosclerotic vascular disease is seen as a mild rise in IMT, which progresses to vascular plaque formation and stenosis. Carotid atherosclerosis, even without significant stenosis, is linked with an increased risk of cerebrovascular disease. Increased IMT in type 2 diabetes can be explained secondary to glucose toxicity to the endothelial layer and glycosylation processes, which is concurred by the greater levels of plasma glucose and HbA1c in diabetic subjects.[30] IMT is also used to evaluate the response to various intervention therapies in atherosclerotic vascular disease.[31–33] It has been postulated that carotid and cerebral arteries and the aorta go through atherosclerotic vascular disease almost at the same time as coronary arteries.[34] Racial differences in CAD morbidity and mortality have been highlighted in previous studies.[19,20,35] Differences between family history of CAD and intima-media thickness in whites and blacks were found in ARIC Study.[36] The importance assessment of intima-media thickness in diverse geographies is highlighted by these ethnic differences. This study assesses CIMT in the central Kerala population. Increased prevalence rates of CAD and diabetes was noted in the south Indian population in various studies.[19,20,37,38] The prevalence of the peripheral vascular disease is low compared to coronary artery disease in the Indian population.[39]

Table 5: Comparison of CIMT with hypertension among diabetic and non-diabetic patients

Diabetes	Hypertension	Mean	SD	N	T	P
Non-diabetic	Absent	0.073	0.016	30	3.36	0.001
	Present	0.090	0.025	75		
Diabetic	Absent	0.085	0.021	22	2.23	0.028
	Present	0.098	0.023	73		

Table 6: Independent predictors of CIMT

	B	Std. Error	T	P	R^2
Age	0.00041	0.00012	3.35	p<0.01	0.389
CHO	0.00022	0.00004	5.69	p<0.01	
HDL	-0.00066	0.00018	3.57	p<0.01	
SBP	0.00023	0.00006	3.92	p<0.01	
Diabetes	0.00868	0.00274	3.17	0.002	

This is an important point of differences in macrovascular disease among Indians and increases the significance of the study on IMT in this population. Increased CIMT is noted in the diabetic group compared with the non-diabetic group in both genders in our study. Females had lesser mean CIMT in comparison to males possibly due to the protecting effect of feminine hormones. Significantly increased IMT in males as compared to females was reported by Kraml et al. [40] Total cholesterol, SBP and DBP showed a statistically significant correlation with CIMT in the non-diabetic group. In the diabetic group, age, total cholesterol, triglycerides, HDL and LDL cholesterol, SBP, DBP and duration of diabetes showed a significant correlation with CIMT. Age, serum cholesterol, HDL cholesterol, SBP and diabetes showed an association with CIMT in multivariate linear regression analysis. An increase in CIMT with the duration of diabetes was seen in our study with a significant p-value of < 0.01. Increased CIMT is noted in the diabetic group as compared with the non-diabetic group in both hypertensive and normotensives in our study. LDL particles because of their adhesion to glycosaminoglycan's in the endothelial basement membrane, causes injury to the endothelium and smooth muscle because of high susceptibility to scavenger receptors on macrophages leading to increased risk of atherosclerotic diseases. [41] Correlation between triglycerides and IMT in diabetics was seen in this study. A good association between triglycerides levels and the progression of IMT has been reported. [41,42] HDL cholesterol was established to be an independent predictor of CIMT values in this study in concurrence with other studies. [43,44] Cholesterol was found to be an independent risk factor for CIMT and showed a correlation with IMT in both diabetics and non-diabetics in our study. Pronounced adverse effects of diabetes and cholesterol on atherosclerotic vascular disease amongst Asian Indians were proposed as a reason for observed increased rates of CVD. [45] Our study showed a correlation of IMT with age in diabetics but not in non-diabetics. This could be due to the predominant older age group in our study.

A higher prevalence of atherosclerotic vascular disease is noted in diabetic patients and carotid atherosclerotic vascular disease sets in around 2-3 decades earlier than non-diabetic subjects. [2] Various studies showed different risk factors for greater CIMT in diabetic subjects. Kawamori et al reported that smoking, duration of diabetes, age, hyperlipidemia and hypertension were independently associated with CIMT in diabetic patients. [2] A study by Geroulakos et al showed that of the likely risk factors none was associated with CIMT in diabetic patients. [46] Merrin et al proposed only age to be an independent risk factor for CIMT. [47] Yamasaki et al found that diabetic mellitus and age to accentuate the atherosclerotic process in the carotid arteries. [48](48) Kanters et al proposed that of the potential risk factors none of the variables were associated with CIMT in Type II diabetes mellitus and identified HbA1c and age as the risk factors for CIMT in Type I diabetes mellitus. [49] IMT also showed predictive power for the risk of stroke and CAD in studies in the elderly population. [10,50] The limitations of this study were relatively small sample size, single-center data, and operator variability in IMT measurement.

Conclusion

We conclude that age, total cholesterol, duration of diabetes and blood pressure exhibited a significant correlation with CIMT. IMT can be considered as a screening aid in diabetic subjects for the early detection of atherosclerosis. Supplemental prospective studies are advocated to assess the retrogression of CIMT with the management of these risk factors among diabetic patients.

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