

Section

General Medicine

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Article

Association Between Carotid Intima Medial Thickness and Dyslipidemia

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ABSTRACT

Background: Objective: The objective was to know the association between carotid intima medial thickness (CIMT) and dyslipidemia.

Methods: The study was carried out in a tertiary care hospital in Kolkata. Total 100 patients were selected randomly who met the inclusion criteria. Among total patients, 48 were males and 52 were females. CIMT was measured by carotid artery ultrasonography using an echo tomography system having midfrequency of 7.5MHz and detection limit of 0.1mm. The blood parameters such as LDL, HDL, total cholesterol, triglyceride and VLDL were estimated by using laboratory technique. Data was collected using a predetermined proforma and statistical analyses were done.

Results: Both common carotid artery IMT and internal carotid artery IMT was increased in a step wise fashion with raising tertiles of LDL ($P < 0.01$) and total cholesterol ($P < 0.01$). There was decreasing trend in both CCA-IMT and ICA IMT with increasing tertiles of HDL ($P < 0.01$). No direct correlation was found between CCA-IMT and ICA-IMT with either VLDL or TG. The mean CIMT was significantly higher in hypertensive subjects than in non-hypertensive subjects. ($P < 0.004$). Mean CIMT was significantly higher in current smokers than in non-smokers ($P < 0.001$).

Conclusions: CIMT is an objective measure of subclinical atherosclerosis, which is a non-invasive, less expensive and time taking and easy reproducible way of demonstrating subclinical atherosclerosis. Thus, it can serve as a window for atherosclerosis status in other major arteries like coronary artery and cerebral arteries. The CIMT is closely associated with dyslipidemia, which can only be identified through specific blood parameters.

Keywords: Carotid intima medial thickness, Dyslipidemia, Blood parameters, Atherosclerosis

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INTRODUCTION

Dyslipidemias are among the major modifiable risk factors for development of atherosclerosis. The carotid intima-media thickness (CIMT) creates prognostic information for future cardio-vascular disease (CVD)¹ and an abnormally increased CIMT as an early indicator of atherosclerosis. According to Abd alamir et al.², common dyslipidemias are combined hyperlipidemia, simple hypercholesterolemia, metabolic Syndrome (MetS), isolated low high-density lipoprotein cholesterol, and isolated hypertriglyceridemia. The dyslipidemia also leads to atherosclerosis due to abnormal fats and lipids in blood. The patients suffering from sequel of atherosclerosis such as coronary artery disease,

myocardial infarction, cerebro-vascular disease meet the clinician at a time when the only treatment option is to minimize the debility already incurred. Moreover, atherosclerosis is responsible for several clinical syndromes that collectively account for large number of morbidity and mortality. Presently, the challenge is to identify the process of atherosclerosis well ahead of patient's symptoms, which can provide us with an opportunity to halt the process of atheroma development and development of plaque vulnerability. To assess the subclinical atherosclerosis various options are available as per researcher.³

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The carotid intima medial thickness was estimated earlier by Pignoli et al.⁴ in which it is measured as the distance from leading edge of first echogenic line to leading edge of second echogenic line in carotid ultrasonography. The first line represents the lumen intimal interphase the collagen containing upper layer of tunica adventitia forms the second line. Extra cranial carotid arteries are superficial, easily accessible and any early change in tunica intima-media of carotid arteries can be easily detected by ultrasonography scanning. It is relatively less expensive, non-invasive, less time consuming and reproducible. CIMT has been used as a subclinical index of atherosclerosis.⁵ Few studies have shown an association between CIMT and dyslipidemia, which lead to myocardial infarction or stroke in elderly or middle-aged subjects² and the study is lacking in West Bengal, India. The study of association between CIMT and dyslipidemia in subjects is of a research interest because the prevalence and incidence of atherosclerotic vascular disease in Indian population is much higher than western population.⁶ Moreover, the measurement of CIMT is serving as a predictor of coronary heart disease which has association with dyslipidemia.² The objective of the present study was to measure the association between carotid intima medial thickness (CIMT) and dyslipidemia.

METHODS

Study area and sample size

The study was conducted in Calcutta National Medical College and Hospital, Kolkata. Total hundred patients were studied those who are having dyslipidemia.

Inclusion Criteria

1. Dyslipidemia after 30 years of age as per important criteria.
2. Patients were asked about the presence of hypertension, dyslipidemia, coronary artery disease, and current smoking habit.

Exclusion Criteria

1. Patients receiving antiplatelet agents.
2. Those receiving lipid lowering drugs.

Measurement of CIMT

Three determinations of IMT were conducted on the site of greatest thickness in common carotid, carotid bulb and internal carotid bilaterally, and these six values were averaged and was used as the representative value for each case.

Assessment of carotid atherosclerosis

Ultrasonographic scanning of carotid arteries were done by using an echotomographic system, Agilent image point HX with an electronic linear transducer (Midfrequency of 7.5 MHz). Scanning of extra cranial common carotid arteries, carotid bulbs, and internal carotid arteries in the neck was performed bilaterally from three different longitudinal projections (i.e. anterior oblique, lateral, posterior oblique) as well as transverse projections as reported in earlier study by Pignoli⁵ and recently studied by Acharyya and Haldar.⁷ All the images were photographed. The scanning session was completed an average of 30 min as per Pignoli.⁵ The detection limit of the echo system was 0.1mm. At each longitudinal projection the site of maximum thickness

including plaque was sought along the arterial wall from the common carotid to internal carotid artery. All scans were conducted by radio diagnosis consultant who was unaware of the clinical characteristic of the subjects.

Assessment of dyslipidemia

Fasting blood was obtained for serum total cholesterol and HDL cholesterol. Serum triglyceride and very low-density lipoprotein (VLDL) was estimated by standardized laboratory techniques. LDL cholesterol was estimated by using the formula of Friedewald et al.⁸

Assessment of hypertension

The hypertension was defined as systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of at least 90 mm Hg or the subject is on pharmaceutical treatment for hypertension.

Assessment of smoking habit

Smoking was defined as smoking more than 1 cigarette per day for at least 1 year, and participants were categorized as never smokers, ever smokers (ceased smoking for at least 6 months), and current smokers.

Statistical analyses

All the data were collected in a prescribed proforma and subsequently analyzed by using statistical software (SPSS, version 20). All the significant value was expressed at $P < 0.05$.

RESULTS

Among 100 subjects, mean age of the study population was 60.39 ± 8.364 years. Among 100 patients, 48 were males and 52 were females.

Study of LDL level and CIMT

The mean LDL-C was 178.98 ± 43.795 mg/dl. In the participants of the study, LDL was measured, and the values were divided in three tertiles (Table 1). In the first tertile, (37-123 mg/dl) there were total 20 subjects 8 were males and 12 were females. The common carotid artery IMT (CCA-IMT) in this group was 0.778 mm. The internal carotid artery IMT (ICA-IMT) was 0.773 mm. In the second tertile (124-154 mg/dl), which included 34 subjects having LDL level between 124 and 154 mg/dl, among them 18 were males and 16 were females. The mean CCA-IMT was 1.386 mm and mean ICA-IMT was 1.418 mm. The third tertile (155-299 mg/dl) contained 46 individuals who had LDL levels between 155 to 299 mg/dl. Among them 22 were males and 24 were females. The CCA-IMT was 1.898 mm and ICA IMT was 1.923 mm. There was increasing trend in both CCA-IMT and ICA-IMT through a stepwise fashion across increasing tertiles of LDL (Fig 1). The association between LDL-C and CCA IMT and ICA IMT is statically significant ($P < 0.01$).

Study of HDL level and CIMT

The mean HDL value was 39.65 ± 16.810 mg/dl. In the participant of the study HDL was measured and the values were divided in three tertiles in accordance with insulin resistance atherosclerosis study (IRAS) (Table 2). In the first tertile (11-37 mg/dl), there were 30 subjects among them 12 were male and 18 were female. Then mean CCA-IMT in this group was 1.975 mm. and mean ICA-IMT was 2.002 mm. In the second tertile (38-48 mg/dl), there were 46 subjects

among them 22 were male and 24 were female. The mean CCA-IMT in this group was 1.575 mm and ICA-IMT was 1.571 mm. In the third tertile (49-125 mg/dl), there were 24 subjects among them 14 were male and 10 were female. The mean CCA-IMT and ICA-IMT in this group were 0.934 mm and 0.876 mm respectively. There was a decreasing trend in both CCA-IMT and ICA-IMT in a stepwise fashion across increasing tertile of HDL (Fig 2). A strong negative correlation between HDL-C and CIMT with a significant level at $P < 0.01$.

Study of total cholesterol level and CIMT

The mean total cholesterol (TC) level was 240 ± 42.812 mg/dl. In the study total cholesterol was divided in three tertiles (Table 3). In the first tertile (< 200 mg/dl), there were 24 subjects among them 6 were males and 16 were females. The mean CCA-IMT and ICA-IMT in this group was 0.925 and 1.067 mm respectively. In the second tertile (200-239 mg/dl), there were 36 subjects among them 20 were males and 16 were females. The mean CCA-IMT and ICA-IMT in this group was 1.438 mm and 1.493 mm respectively. In the third tertile (≥ 240 mg/dl), there were 40 subjects 20 among them were males and rest 20 were females. The mean CCA-IMT and ICA-IMT in this group were 1.727 mm and 1.721 mm respectively. There was an increasing trend in both CCA-IMT and ICA-IMT in a stepwise fashion across increasing tertiles of total cholesterol (Fig 3). The TC was significantly ($P < 0.01$) associated with CIMT.

Study of triglyceride level and CIMT

In the present study triglyceride (TG) level was divided in three tertiles (Table 4). In the first tertile (23-94 mg/dl), there were 10 subjects, 4 among them were males and 6 were females. The mean CCA IMT and ICA IMT in these groups were 0.787 mm, and 0.776 mm. In the second tertile (95-154 mg/dl), there were total 33 subjects and 18 among them were males and 6 were females. Mean CCA IMT and ICA IMT in these groups were 1.807 and 1.652 mm respectively. In the third tertile (155-1023 mg/dl), there were 57 subjects among them 26 were males and 31 were females. The mean CCA IMT and ICA IMT in these groups were 1.045 and 1.033 mm. There was no stepwise increase in CCA IMT or ICA IMT across the TG tertiles. The CCA IMT in top tertile is 0.752 mm thinner than the second tertile. The ICA IMT in the top tertile is 0.619 mm thinner than the second tertile. No statistically significant correlation between TG and CIMT was found ($P = 0.49$).

Study of VLDL level and CIMT

In the study, VLDL was divided in three tertiles (Table 5). In the first tertile (1-13 mg/dl), there were 20 subjects among them 8 were males and 12 were females. The mean CCA IMT and ICA IMT in these groups were 1.090 mm and 0.969 mm respectively. In the second tertile (14-26 mg/dl), these were 32 subjects among them 18 were males and 14 were females. The mean CCA IMT and ICA IMT were 1.733 mm and 1.894 mm respectively. In the third tertile (27-200 mg/dl), there were 48 subjects among them 20 were males and 28 were females the mean CCA IMT and ICA IMT in this group were 1.420 mm and 1.340 mm. There is no stepwise gradual relationship between increasing VLDL and CCA IMT or ICA IMT. The CCA IMT in the top tertile is 0.313 mm thinner than the second tertile. The ICA-IMT in the top tertile is 0.554 mm thinner than the second tertile. No statistically significant correlation between VLDL and CIMT was found ($P = 0.49$).

Study of hypertension and CIMT

In this study, hypertension was defined as systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of at least 90 mm Hg or the subject is on pharmaceutical treatment for hypertension. Based on these criteria, among 100 subjects 59 nos. were hypertensive. Among them 30 were males and 29 were females. The mean CIMT in this group was 1.655 mm. There were 41 non hypertensive subjects among them 18 were males, and 23 were females. Mean CIMT in this group was 1.322 mm. The mean CIMT in hypertensive subjects was, 0.333 mm thicker than non-hypertensive subjects. It was observed the hypertension was significantly ($P < 0.004$) associated with CIMT (Table 6).

Study of smoking habit and CIMT

Among 48 male subjects, 36 were smokers and 12 were non-smokers, among 36 smokers, 20 were current smokers and 16 were former smokers (Table 7). Among females, none were smokers. The mean CIMT in current smoker was 1.848 mm and in the former smoker mean CIMT was 1.516 mm. Those subjects who were never smokers had mean CIMT of 0.949 mm. Smoking habit was significantly ($P < 0.001$) associated with CIMT.

Table 1: Association between LDL and CIMT

LDL (mg/dl)	N	Males	Females	CCA IMT (mm)	ICA IMT (mm)	P value
37-123	20	8	12	0.778	0.773	
124-154	34	18	16	1.386	1.418	< 0.01
155-299	46	22	24	1.894	1.923	

Table 2: Association between HDL and CIMT

HDL (mg/dl)	N	Males	Females	CCA IMT (mm)	ICA IMT (mm)	P value
11-37	30	12	18	1.975	2.002	
38-48	46	22	24	1.575	1.571	< 0.01
49-125	24	14	10	0.934	0.876	

Table 3: Association between TC and CIMT

TC (mg/dl)	N	Males	Females	CCA IMT (mm)	ICA IMT (mm)	P value
< 200	24	8	16	0.925	1.067	
200-239	36	20	16	1.438	1.493	< 0.01
≥ 240	40	20	20	1.727	1.721	

Table 4: Association between TG and CIMT

TG (mg/dl)	N	Males	Females	CCA IMT (mm)	ICA IMT (mm)	P value
23-94	10	4	6	0.787	0.776	
95-154	33	18	15	1.807	1.652	$= 0.49$
155-1023	57	26	31	1.045	1.033	

Table 5: Association between VLDL and CIMT

VLDL (mg/dl)	N	Males	Females	CCA IMT (mm)	ICA IMT (mm)	P value
1-13	20	8	12	1.090	0.969	
14-26	32	18	14	1.733	1.894	$= 0.49$
27-200	48	20	28	1.420	1.340	

Table 6: Association between hypertension and CIMT

Blood pressure	N	Males	Females	Mean CIMT (mm)	P value
Non hypertensive	41	18	23	1.322	<0.004
Hypertensive	59	30	29	1.655	

Table 7: Association between smoking habit and CIMT

Smoking status	N	Mean CIMT (mm)	P value
Current	20	1.848	<0.001
Former	16	1.516	
Never	12	0.949	

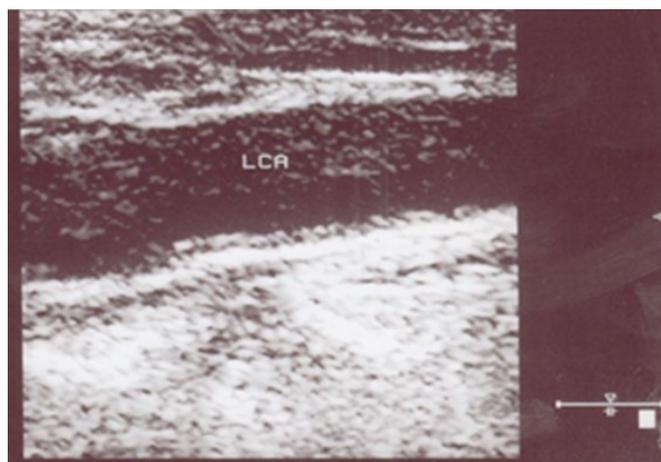


Fig 1: Thickened intima media of LCA

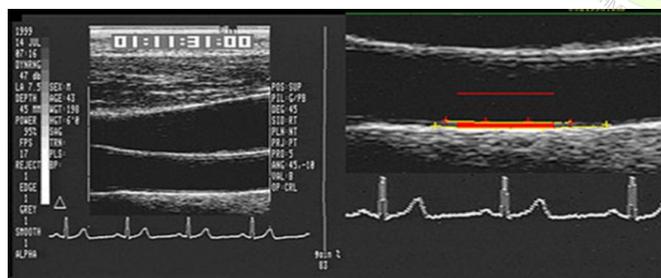


Fig 2: Thickened CIMT

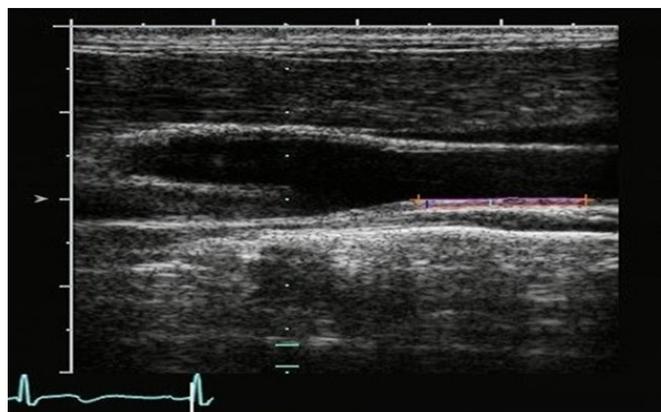


Fig 3: Thickened CIMT

DISCUSSION

In the present study, specific objective of the study was to assess the association between carotid intima medial

thickness (CIMT) and pattern of dyslipidemia. CIMT is an objective measure of subclinical atherosclerosis as per several researchers.^{2,7,9-12} The study was also conducted to verify the role of CIMT in assessment of subclinical atherosclerosis along with pattern of dyslipidemia. It has already been established that several factors such as aging, hypertension, dyslipidemia, duration of diabetes, and smoking habits were closely associated with increasing of CCA IMT.¹³

Both common carotid artery IMT and internal carotid artery IMT was increased in a step wise fashion with raising tertiles of LDL (P<0.01) and total cholesterol (P<0.01). There is decrease in both CCA IMT and ICA IMT with increasing tertiles of HDL (P<0.01). No direct correlation was found between CCA IMT and ICA IMT with either VLDL or TG. The mains abnormality is moderately raised triglyceride and decreased HDL cholesterol; LDL and total cholesterol a powerful predictor of cardiovascular risk in non-diabetic population may be normal or slightly raised. But in Indian diabetic dyslipidemic patient LDL is raised, HDL is reduced, and triglyceride is increased; that is why changes of atherosclerosis are increased.

The over production of triglyceride rich VLDL by the liver and impaired triglyceride clearance via lipoprotein lipase are contributory factors in diabetic dyslipidemia. Increased lipid exchange with triglyceride rich lipoproteins favor the production of small dense LDL, which is recognized by specific receptors in arterial wall, which is highly atherogenic and small dense HDL (HDL3) which is less atherogenic than relatively depleted HDL2.

The mean CIMT was significantly higher in hypertensive subjects compared to non- hypertensive subjects (P<0.004). The present study results also are in conformity with the earlier study done by Puato et al.¹¹ They documented that increase in carotid intima media thickness in grade I hypertensive subjects and. the levels of mean arterial pressure at 24hr monitoring and total serum cholesterol were factors potentially linked to the increment in mean IMT. No differences were found between white coat hypertensive subjects and sustained hypertensive subjects for mean IMT. According to them, carotid IMT is greater and grows faster in white coat hypertensive subjects than in normotensive subject, without significant differences with sustained hypertensive patients.

Mean CIMT was significantly higher in current smokers and former smokers than never smokers (P<0.001). This present result is in conformity with the earlier study that smoking status increased CIMT and it was observed for both men and women, current smoking was associated with thicker echogenic layer compared to never smokers.¹⁴ It was also observed that in previous study that former smokers exhibited thinner echogenic layer than current smokers after adjustment for cigarette pack year. The atherogenic effect of smoking appears to be partly reversible among former smokers.¹⁵⁻¹⁶

CONCLUSION

CIMT may be an indicator of endothelial dysfunction and can well become in future an independent risk factor for coronary heart disease and cerebrovascular accidents. So, CIMT may be our objective measure of macro vascular disease in future, depending on which the future doctors will tailor their therapy for atherosclerosis. However, the present study

proved that dyslipidemia in subjects may lead to atherosclerosis due to increased CIMT.

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Ethical approval

The ethical approval has been given by Institutional Ethical Committee, Calcutta National Medical College and Hospital, Kolkata, India. The ethical committee have given the written permission with Memo No. CNMC/ETHI/1653/P dated 13/02/2007 for conducting the present research work.

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