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Correlation of blood sugar and lipid parameters with carotid intima media thickness among patients with type II diabetes mellitus

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Background: Of the various non invasive imaging methods available, arterial intima media thickness measurement obtained by B mode ultrasound is currently recommended by the American Heart Association as being relatively safe, non invasive and inexpensive method of assessing sub clinical atherosclerosis, and being an independent predictor of atherosclerotic events. **Aim:** To study the correlation between glycemic and lipid levels with carotid intima media thickness among patients with type II diabetes mellitus. **Methodology:** A prospective longitudinal study was conducted for a period of one year. Patients in the age group of 30 to 70 years with type II diabetes for more than 2 years were included as our study subjects. A total of 100 patients were included as our study subjects. Anthropometric measurements, blood sugar parameters and lipid parameters were measured as per the guidelines. Carotid artery intima media thickness was measured by B mode ultrasound having an electric transducer with a mid frequency of 7.5 MHz. **Results:** A multivariate analysis was performed to assess the various factors influencing the increase in the thickness of CIMT and among that we found a significant correlation had occurred with the factors like BMI, waist hip ratio, fasting and post-prandial blood sugar, HbA1C and among the lipid parameters LDL, total cholesterol and triglycerides had shown a statistical significant correlation ($p<.05$), whereas factors like age, gender, hypertension status, duration of diabetes and HDL cholesterol among the lipid parameter did not show a statistical significant correlation with CIMT ($p>.05$). **Conclusion:** CIMT measurement can be used as a regular screening tool in diabetic patients for the early detection of atherosclerosis among them.

Keywords: Carotid intima media thickness, Lipid parameters, Blood glucose parameters, Correlation

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Introduction

Globally, due to the demographic transition where the population of aged people was found to have a sharp increase over the past few decades, we also found a change in the epidemiology of diseases in which the prevalence of infectious diseases was found to come down and the prevalence of non-communicable diseases had shown a steady increase. In India among the various non-communicable diseases coronary artery disease is one of the most common ailments, as per the 2013 data deaths due to cardiovascular diseases accounts to one third of all deaths occurring globally [1,2].

Diabetes considered being a major risk factor for CVD due to its oxidative stress on the endothelial walls and thereby causing endothelial dysfunction and consequently leading onto thickening of intima media [3]. Dyslipidemia with high triglycerides and LDL cholesterol and low HDL cholesterol, in type II diabetes patients would be a triggering factor in the development of atherosclerosis [4]. Carotid Intimal Medial Thickness (CIMT) is the area of tissue starting at the luminal edge of the artery and ending at the boundary between the media and the adventitia and it is a measure of subclinical atherosclerosis associated with cardio-vascular risk factors (CVRFs) and is predictive of stroke incident [5-8].

In healthy middle-aged adults it measures 0.6 to 0.7 mm and greater than 1.20 mm is considered abnormal. CIMT is age-dependent and increases at a rate of 0.005 to 0.010 mm/year [9]. Increase in CIMT can predict future events of silent brain infarction and coronary heart disease [10]. Of the various non invasive imaging methods available, arterial intima media thickness measurement obtained by B mode ultrasound is currently recommended by the American Heart Association as being relatively safe, non invasive and inexpensive method of assessing sub clinical atherosclerosis, and being an independent predictor of atherosclerotic events [11].

So, detection of atherosclerosis in the early phase by using CIMT is effective in arresting the progression of the disease by doing an early intervention and very few Indian studies had seen the association between CIMT and dyslipidemia and as well with diabetes and so the present study was conducted to assess and correlate the CIMT values with the glycemic levels and the lipid levels.

Aim

To study the association between glycemic and lipid levels with carotid intima media thickness among patients with type II diabetes mellitus.

Methodology

Study setting and study type: A prospective longitudinal study was conducted for a period of one year between April 2017 and March 2018 in our medical college hospital.

Ethical consideration: The study was started after getting the approval from the institutional ethical committee.

Inclusion criteria: Patients in the age group of 30 to 70 years with type II diabetes for more than 2 years were included as our study subjects.

Exclusion criteria: Type I diabetes patients and patients with history of coronary artery disease (CAD), cerebrovascular disease (CVD), chronic kidney disease (CKD) and primary dyslipidemia were excluded from the study. Patients with history of alcohol and smoking were also excluded from the study.

Sampling method and sample collection: A total of 100 patients were included as our study subjects based on non-random quota sampling. Informed consent was obtained from all the patients involved in our study. A detailed history related to their diabetes status and risk factors was obtained from all patients and a complete general physical examination was conducted on all study subjects. Anthropometric measurements like BMI, waist hip ratio and blood pressure were measured on all patients based on routine guidelines. The fasting venous plasma glucose (FBS) and fasting lipid profile (FLP) were obtained after 12 hours of overnight fasting using the Olympus AU-400 Auto Analyzer and the 2 hour post prandial venous plasma glucose (PPBS) estimation was also done. The value of LDL was calculated using Freidewald's formula when the triglyceride was less than 400mg/dl and direct estimation was done when the triglyceride was more than 400mg/dl. Dyslipidemia was defined based on National cholesterol education programme ATP 111 guidelines and the normal cut off values were taken as total cholesterol less than 200mg/dl; LDL less than 100mg/dl; triglyceride less than 150mg/dl and values outside these limits were considered as abnormal.

For HDL cholesterol a value less than 40mg/dl was considered low and more than or equal to 60mg/dl was considered high as per the ATP111 guidelines. HbA1c was estimated by column chromato-graphy method.

The patients were categorized as those having a HbA1c of less than 8% which indicates good control of diabetes and those having more than 8% which indicates poor control of diabetes. Carotid artery intima media thickness was measured by B mode ultrasound having an electric transducer with a mid frequency of 7.5 MHz. Scans were performed on both the right and left extracranial carotid arteries by trained personnel.

The IMT values were measured in six well defined arterial segments- near wall and far wall of distal 6mm of common carotid, the carotid bulb and proximal 6mm of internal carotid artery of both sides. The final IMT considered was the average of the IMT values at the 12 sites examined. Since IMT is considered as a candidate marker of cardiovascular risk, its normal value is interpreted in terms of increased risk rather than in terms of statistic distribution within a population. An upper limit of 0.9mm was chosen for the present study based on epidemiological data currently available.

Statistical analysis: All data were entered and analysed using SPSS version 22. Mean and standard deviation was derived for all parametric variables and percentage was calculated for all parametric variables. Chi-square test was used to study the association between the two variables and pearson's correlation was used to assess the correlation between CIMT and lipid parameters and similarly CIMT and blood sugar parameters.

Results

The age wise distribution of the study subjects shoed that majority of the type II diabetes patients were in the age group between 40 and 60 years and the mean age was 55 years among males and 54 among females and there was almost near equal distribution of male and female patients (table 1).

Table-1: Age and gender wise distribution of the study subjects.

Age	Male	Female	Total	p value
30 – 40	2 (4%)	4 (8%)	6 (6%)	0.726
41 – 50	17(34.6%)	12 (23.5%)	29 (29%)	
51 – 60	14 (28.5%)	25 (49%)	39 (39%)	
61 – 70	16 (32.6%)	10 (19.6%)	26 (26%)	
Total	49 (100%)	51 (100%)	100 (100%)	
Mean ± SD	55.5±9.3	54.8±8.4		

Table-2: Distribution of the study subjects based on the duration of diabetes.

Duration of diabetes in years	Frequency	Percentage	Mean	SD
3 – 5	60	60%	4.65	3.9
5 – 7	16	16%		
7 – 9	10	10%		
9 – 11	7	7%		
11 – 13	3	3%		
>13	4	4%		
Total	100	100%		

In our study we included the patients with the history of diabetes for more than two years and more than 50% of them had the diabetes history between 3 and 5 years and the maximum duration was up to 15 years and the mean duration was 4.5 years (table 2).

Table-3: Mean and SD of the various blood parameters measured among the study subjects.

Blood parameter	Mean (mg/dl)	SD
Fasting blood sugar	162.2	69.6
Post-prandial blood sugar	254.7	91.4
HbA1c	7.35 gms%	0.86
Total cholesterol	243.9	72.4
Triglycerides	184.5	67.4
LDL	150.4	62
HDL	47.5	4.3

The mean of the various blood sugar and lipid parameters measured among the diabetes patients was shown in table 3 with a mean fasting, post-prandial and HbA1C values of 162mgs/dl, 254 mgs/dl and 7.3 gms % respectively and similarly all the lipid parameters like total cholesterol, triglycerides and LDL cholesterol was found to be above normal except for HDL which was found to be in normal limits.

Table-4: Mean and SD of CIMT of both sides.

CIMT	Mean (mm)	SD
CIMT right side	0.80	0.52
CIMT left side	0.84	0.55

The carotid intima media thickness was measured among both sides and the mean CIMT of right side was 0.80 mm and in left side it was 0.84 mm and the thickness was almost similar among both sides (table 4).

Table-5: Association and correlation between CIMT and blood sugar parameters.

Blood sugar parameter	CIMT (right side)		CIMT (left side)	
	Correlation *	Association**	Correlation *	Association**
FBS	0.237	<.0001	0.224	<.0001
PPBS	0.314	<.0001	0.323	<.0001
HbA1C	0.370	<.0001	0.368	<.0001

*-correlation was assessed using pearson's correlation

**- association was assessed using unpaired T test

Carotid intima media thickness was found to have a strong significant statistical association with the blood sugar parameters whereas correlation shows only a weak positive correlation between these two parameters and similarly association between CIMT and lipid parameters had shown a significant association and the correlation was almost similar to the blood sugar parameters (table 5 and 6)

Table-6: Association and correlation between CIMT and lipid parameters.

Lipid parameter	CIMT (right side)		CIMT (left side)	
	Correlation *	Association**	Correlation *	Association**
TC	0.284	<.0001	0.281	<.0001
Triglycerides	0.220	<.0001	0.219	<.0001
LDL	0.279	<.0001	0.282	<.0001
HDL	-0.103	<.0001	0.110	<.0001

*-correlation was assessed using pearson's correlation

**- association was assessed using unpaired T test

Table-7: Multivariate analysis of factors influencing the carotid intima media thickness.

Factor	Co-efficient	Std. error	F test	P value
Age	0.205	0.144	0.781	0.349
Gender	0.139	0.098	0.709	0.298
Duration of diabetes	0.219	0.129	0.665	0.0721
BMI	0.321	0.133	3.865	0.017
W/H ratio	0.336	0.165	3.590	0.005
Hypertension	0.199	0.082	0.928	0.199
FBS	0.237	0.142	2.995	0.0431
PPBS	0.314	0.168	3.517	0.0217
HbA1C	0.370	0.121	3.918	0.0210
LDL	0.279	0.151	2.981	0.0287
TC	0.284	0.067	3.126	0.0265
Triglycerides	0.220	0.187	2.109	0.0487
HDL	-0.103	0.132	1.092	0.0921

A multivariate analysis was performed to assess the various factors influencing the increase in the thickness of CIMT and among that we found a significant correlation had occurred with the factors like BMI, waist hip ratio, fasting and post-prandial blood sugar, HbA1C and among the lipid parameters LDL, total cholesterol and triglycerides had shown a statistical significant correlation ($p<.05$), whereas factors like age, gender, hypertension status, duration of diabetes and HDL cholesterol among the lipid parameter did not show a statistical significant correlation with CIMT ($p>.05$) (table 7).

Discussions

The detection of atherosclerosis in an early stage can be done by suing ultrasound B mode by measuring the carotid intima media thickness in asymptomatic patients with cardiovascular diseases. Previous studies had proven that the thickness of CIMT as an individual predictor for atherosclerosis and had also identified certain factors responsible for the increase in thickness and in the present study we tried to associate and correlate the values of blood sugar and lipid parameters with that of the CIMT [12,13]. The mean CIMT in the present study was found to be 0.83 mm and it was found to be slightly higher among males than the females. Similar type of study done in Chennai had shown the mean value of CIMT as 0.95 mm and a study done by Gayathri et al had shown the mean CIMT value as 0.935 [14]. Females had a relatively lower value of CIMT as compared to males possibly due to the protective effect of female hormones and/or male gender being at a higher risk of atherosclerosis. Similar results have been reported by Kraml et al who also observed significant higher IMT in men than women [15]. The present study showed that the anthropometric measurements mainly the BMI and waist hip ratio had shown a statistical significant correlation with CIMT values and a similar type of results was also shown by Masoud Manaviat et al [16]. A study by Frouse et al on association of obesity and central fat distribution with carotid artery wall thickening had shown an independent association between general and abdominal obesity reflected by high BMI and WHR respectively and carotid wall thickening [17]. Waist hip ratio was found to be an independent determinant of intima media thickness even after multivariate analysis. Our study had shown a significant association and correlation between various blood sugar parameters like FBG, PPBG and HbA1c with the CIMT values.

The relationship between the level of FBG and CIMT has been controversial. Previous studies have shown that there was no significant association between IFG and CIMT after adjustment by covariates [18,19].

The associations between hyperglycemia and CIMT were significant in univariate analyses, but disappeared after adjustment for age, sex and anthropometric variables [20,21]. Furthermore, other studies have shown that higher HbA1c levels were significantly and independently related to increased CIMT, but IFG was not [22,23].

The most recent study in community dwelling Japanese older adults showed that elevated IFG was significantly associated with increased CIMT [24]. Consistent with that study, in the present study, we found a significant relationship between FBG and mean CIMT. The current study had proven that after multivariate analysis the correlation between the various lipid parameters like LDL, total cholesterol and triglyceride levels had shown a statistical significant correlation with CIMT.

Previous studies have also shown that low apolipoprotein A1 levels, and elevated LDL-C and apolipoprotein B levels in childhood predict increased CIMT in adulthood, and that a high LDL-C concentration predisposes to the progression of subclinical atherosclerosis [25,26].

LDL particles have been suggested to predict an increased risk of atherosclerotic diseases because of their toxicity to the endothelium and underlying smooth muscle, adhesion to glycosaminoglycans in the endothelial basement membrane, and high susceptibility to scavenger receptors on macrophages [27].

However, the association between TG and CIMT has been unclear, especially in low-income populations. Numerous studies have shown that there was a positive association between TG and CIMT; two longitudinal studies reported a positive association between baseline TG levels and progression of CIMT [27,28].

Among the various lipid parameters in our study we didn't find a strong negative correlation between HDL cholesterol and the CIMT values and a similar type of results was also established in a Chinese study done by Liu Gao etal and most of the other studies had also proven that no significant correlation had existed between the HDL levels and the CIMT values.

Conclusion

As of today the prevalence of atherosclerosis among diabetes patients are in an increasing trend. Assessment of carotid artery intima media thickness by B mode ultrasound is a proxy measure for early detection of atherosclerosis and also a more cost-effective tool and so early interventions can be taken in preventing major complications like stroke or cardiovascular diseases. Both the blood sugar and the lipid parameters had a statistical significant correlation with carotid intima media thickness along with BMI and waist hip ratio, whereas age, gender, hypertension status and duration of diabetes did not show any association with CIMT. So CIMT measurement can be used as a regular screening tool in diabetic patients for the early detection f atherosclerosis among them.

Contribution by authors

01. **Kirubhakaran Kanakaraju:** data collection and preparing the manuscript
02. **Rangabashyam Seetharaman Ranganathan:** methodology preparation and helping in manuscript writing
03. **Dr R Shankar:** statistical analysis and deriving statistical inference.

What this study adds to the existing knowledge

Measuring the carotid intima media thickness and correlating it with blood sugar levels and lipid parameters would help in detecting the atherosclerosis in the early phase among type II diabetes patients.

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