European Journal of Molecular & Clinical Medicine

ISSN: 2515-8260, Volume 10, Issue 05, 2023

ASSOCIATION OF CAROTID INTIMA MEDIA THICKNESS WITH CARDIO VASCULAR RISK FACTORS IN TYPE 2 DIABETES MELLITUS PATIENTS – A CROSS SECTIONAL STUDY

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ABSTRACT

Background: Cardiovascular disease is the number one cause of morbidity and mortality in diabetic patients. Sonography has made it easier to study subclinical atherosclerosis by determining the Carotid Intima-Media Thickness. **Aim:** To investigate the significance of Carotid Intima Media Thickness (CIMT) in prediction of cardio vascular risk in Type 2 Diabetes Mellitus (T2DM) patients. **Method**: A total of 110 T2DM patients aged 34-96 years (mean age 54.57±10.66 years; 50% males) were enrolled in the study. Demographic details, diabetic history, level of glycemic control, anthropometric assessment, lipid profile and blood pressure were assessed. Metabolic syndrome was assessed using the IDF criteria. CIMT was assessed sonographically. CIMT >0.9 mm in either of two sides was considered as abnormal. Data was analyzed using Chi-square and Student 't'-test. **Results:** Mean CIMT was 0.81±0.22 mm. There were 46 (41.8%) patients with abnormal CIMT. Prevalence of Metabolic syndrome was 73.6%. A significant association of abnormal CIMT was seen with older age, male sex, longer duration of diabetes, diabetic treatment incorporating both insulin and oral hypoglycemic agents, blood sugar levels (both fasting and post-prandial), higher HbA1c and poor glycemic control. Among traditional cardiovascular risk factors, abnormal CIMT showed a significant association with obesity (WC and WHR), smoking habit, higher blood pressure/hypertension, higher lipid levels (TC, TG, LDL) and metabolic syndrome. **Conclusion**: There was a high prevalence of CIMT abnormalities in the T2DM patients which was related with demographic, disease related factors and other traditional cardiovascular risk factors. Further studies with inclusion of a control group are also recommended.

Key words: Type 2 Diabetes mellitus, Cardiovascular risk factors, Carotid Intima Media thickness, Metabolic syndrome.

1. INTRODUCTION

Lifestyle disorders happen to be the most common challenge for the mankind and probably are the most common non-infectious threat to health. Among various lifestyle disorders, diabetes appears to have most widespread impact both in terms of persons affected

as well as its ability to trigger in other health-related risks. As per an estimate, it affects nearly 6.28% of total population of the world[1].

Several factors in the development of atherosclerosis and cardiovascular disease are often comorbid in individuals with Type 2 Diabetes which include hypertension, insulin resistance, hyperglycemia, obesity and dyslipidemia[2]. Owing to these metabolic implications, the comorbidity burden in diabetic patients is quite high[3,4]. In view of the high risk of cardiovascular disease in diabetic patients, the focus of diabetes care is on early identification and management of cardiovascular disease, preferably at subclinical stage itself.

Sonography has made it easier to study subclinical atherosclerosis by determining the Carotid Intima-media thickness (CIMT). Carotid Intima Media Thickness is considered a biomarker of atherosclerosis and is associated with overall CVD risk, particularly in those with Type 2 Diabetes[5]. The high-resolution, non-invasive B-mode ultrasonography is one of the best methods for the detection of early stages of atherosclerotic disease[6]. For every 0.1-mm increase in carotid IMT, the relative risk of ischemic heart disease increases by 15% and that of cerebrovascular disease by 18%7.

Considering the significance of carotid intima media thickness in assessment and stratification of cardiovascular risk in diabetic patients, the present study was planned to study the association of carotid intima media thickness with cardio vascular risk factors in type 2 diabetes mellitus patients.

2. METHOD

This cross-sectional study was carried out after getting institutional ethical committee clearance in AVMCH for a period of 2 years from November 2020 to October 2022. Patients with Type 2 Diabetes Mellitus with age more than 30 years, of either sex, receiving Anti-Diabetic drugs or insulin or both were included in the study. Patients with Chronic kidney disease, Thyroid disease, Liver disease, Rheumatoid disease, Coronary Artery Disease, Hypertension, Cerebrovascular accident and Familial Hypertriglyceridemia were excluded in the study. A total of 110 patients were included after applying inclusion and exclusion criteria.

At enrolment, demographic details, duration of diabetes and type of treatment being taken were noted. A history of personal habits (smoking and alcohol use) was obtained.
Systolic/Diastolic blood pressure >130/85 was considered as cardiovascular risk[8]. Glycemic control stratification was done using the following criteria[9]:
<6.5% -Well controlled, 6.5-8.0% - Fair controlled, >8% - Poorly controlled
Cardiovascular risk on the basis of lipids was assessed using the following criteria:

Total cholesterol (TC)	$\geq$210 mg/dl[10]
Triglyceride (TG)	>150 mg/dl[8]
High density lipoprotein	<50 mg/dl in females <40 mg/dl in males[8]
Low density lipoprotein	>130 mg/dl[10]

Central obesity based on WHR criteria was determined on the basis of World Health Organization recommendations that consider WHR>0.85 as abnormal for females and WHR >0.90 as abnormal for males[11].

The Carotid Intima Media Thickness was measured by high-resolution B mode system with linear ultrasound transducers at frequencies 7 MHz – 12MHz. It is measured between the intimal-luminal and the medial-adventitial interfaces of the carotid artery. The space between the two hyperechoic lines (the “double-line”) corresponds to Intima Media Thickness[12]. The Carotid Intima Media Thickness (CCA-IMT) was usually measured in the common carotid artery on the far wall proximal to the bifurcation. The cut-

off value for determination of a thickened or abnormal CIMT was taken as >0.9[13]. CIMT of both right and left sides was measured. Average CIMT was calculated from the two. An abnormal CIMT was considered if either of two measurements was above the cut-off level.

3. STATISTICS

The collected data were entered in Microsoft Excel and was analyzed using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. Descriptive statistics (mean, standard deviation) were used to describe continuous variables, while proportion were used for categorial variables. Association between continuous variable were obtained using T test and association between categorial variable were obtained using chi square test. A p value of less than 0.05 has been considered to be significant.

4. RESULT

The present study was carried out to assess carotid intima media thickness in Type 2 diabetes mellitus (T2DM) patients and to assess its association with different cardiovascular risk factors.

A total of 110 T2DM fulfilling the eligibility criteria of the study were enrolled and the mean age of patients was 54.57±10.66 years. The sex-ratio (M:F) of the study was 1:1.

In our study, Duration of diabetes ranged from 1 to 29 years with a mean of 8.44±5.69 years. Majority of patients were on oral hypoglycemic agents (68.2%), only 5.5% were on insulin and 26.4% patients were on both insulin and OHAs. Mean fasting, postprandial blood sugar and HbA1c levels were 155.65±66.77 mg/dl, 232.31±84.95 mg/dl and 7.26±1.43% respectively. Good, fair and poor glycemic control on the basis of HbA1c was 30.9%, 51.8% and 17.3% respectively.

77.3% patients were obese as per waist circumference criteria and as per waist-hip ratio criteria, there were 32.7% obese patients. In this study, there were 30% alcoholics and 34.5% smokers. There were 50.9% patients with hypertension. Hypertriglyceridemia and low HDL were seen in 59.1% and 60% patients respectively.

Mean CIMT of left and right sides was 0.80±0.21 and 0.82±0.23 mm respectively among the patients in the study and the average CIMT was 0.81±0.22 mm. Of the total 110 patients, 41.8% patients had abnormal CIMT of >0.9 mm.

Table 1: Association of CIMT with demographic and diabetic profile of patients

SN	Characteristic	Abnormal CIMT (n=46)	Normal CIMT (n=64)	Statistical significance
1.	Mean age±SD (years)	61.24±9.82	49.78±8.48	t=6.540; p<0.001*
2.	Male:Female	29(63.0%): 17(37.0%)	26(40.6%): 38(59.4%)	χ^2=5.380; p=0.020*
3.	Mean duration of diabetes±SD (years)	11.52±5.84	6.22±4.44	t=5.411; p<0.001*
4.	Type of Treatment			
	OHAs	16 (34.8%)	59 (92.2%)	χ^2=41.733; p<0.001*
	Insulin	4 (8.7%)	2 (3.1%)	
	Both	26 (56.5%)	3 (4.7%)	
5.	Mean FBS±SD (mg/dl)	192.46±85.89	129.19±27.34	t=5.525; p<0.001*
6.	Mean PPBS±SD (mg/dl)	286.41±99.37	193.42±41.94	t=6.710; p<0.001*

7.	Mean HbA_{1c}±SD (%)	8.10±1.56	6.66±0.97	t=5.970; p<0.001*
8.	Level of glycemic control			
	Good	1 (2.2%)	33 (51.6%)	χ^2=32.751; p<0.001*
	Fair	31 (67.4%)	26 (40.6%)	
	Poor	14 (30.4%)	5 (7.8%)	

Statistical test used – student t test and chi square test
***p value <0.05 – statistically significant**

Table 2: Association of CIMT with central obesity parameters, blood pressure, lipid profile parameters and personal habits

SN	Characteristic	Abnormal CIMT (n=46)		Normal CIMT (n=64)		Statistical significance	
1.	Central Obesity parameters						
	Mean WC±SD (cm)	97.28±6.73		91.09±7.68		t=4.389; p<0.001*	
	Mean WHR±SD	0.90±0.08		0.86±0.06		t=2.940; p=0.004*	
2.	Blood Pressure						
	Mean SBP±SD (mmHg)	136.30±13.39		122.19±12.28		t=5.727; p<0.001*	
	Mean DBP±SD (mmHg)	89.57±7.88		79.52±10.29		t=5.556; p<0.001*	
	No. of patients with hypertension as per IDF criteria (%)	35 (76.1%)		21 (32.8%)		χ^2=5.582; p=0.018*	
3.	Lipid profile parameters						
	Mean TC±SD (mg/dl)	188.80±41.49		155.19±22.80		t=5.414; p<0.001*	
	Mean TG±SD (mg/dl)	207.59±74.14		149.89±42.61		t=5.130; p<0.001*	
	Mean HDL±SD (mg/dl)	42.35±9.07		41.87±8.21		t=0.285; p=0.776	
	Mean LDL±SD (mg/dl)	104.98±31.56		83.27±17.59		t=4.577; p<0.001*	
4.	Personal Habits	**No.**	**%**	**No.**	**%**	χ^2	P
	Smoking	22	47.8	16	25.0	6.167	0.013*
	Alcohol	18	39.1	15	23.4	3.139	0.076*

Statistical test used – chi square test, *p value <0.05 – statistically significant

In the present study, we found a significant association of older age, male sex, longer duration of diabetes, diabetic medication (OHA+insulin), poor glycemic control, larger waist hip ratio, central obesity as per waist circumference, smoking habit, hypertensive status and higher mean systolic and diastolic blood pressures and dyslipidemia with CIMT abnormality (Table 1-2). It is hence recommended that periodic CIMT assessment should be included as a routine follow-up outcome in diabetic patients.

Table 3: Predictors of CIMT by Multivariate analysis

Coefficients[a]								
Model		**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**	**95.0% Confidence Interval for B**	
		B	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
1	(Constant)	-.732	.216		-3.386	0.001	-1.162	-.303
	Age (yrs)	.010	.001	.517	7.258	<0.001*	.008	.013
	WC (cm)	.007	.002	.246	3.673	<0.001*	.003	.010
	WHR	-.110	.208	-.038	-.532	.596	-.523	.302
	SBP(mmHg)	-.001	.001	-.045	-.450	.654	-.004	.002
	DBP(mmHg)	.004	.002	.177	1.902	.060	.000	.007
	FBS (mgdl)	.001	.000	.253	1.945	.055	.000	.002
	PPBS(mgdl)	-8.834E-005	.000	-.035	-.238	.813	-.001	.001
	HbA1c	.013	.013	.088	.994	.323	-.013	.040
	TC (mgdl)	.004	.013	.635	.289	.773	-.021	.029
	TG (mgdl)	.000	.003	-.135	-.168	.867	-.005	.005
	HDL (mgdl)	-.006	.013	-.222	-.448	.655	-.031	.019
	LDL(mgdl)	-.003	.013	-.400	-.252	.801	-.028	.022
a. Dependent Variable: AvCalc								

In a multivariate model where average CIMT was considered as a dependent on age, waist circumference, WHR, SBP, DBP, FBS, PPBS, HbA_{1c}, Total cholesterol, Triglyceride, HDL and LDL, only age and waist circumference emerged as significant predictors of CIMT (Table 3).

Figure 1&2 show ultrasonographic images of Normal and increased CIMT which was taken in different patients during the study.

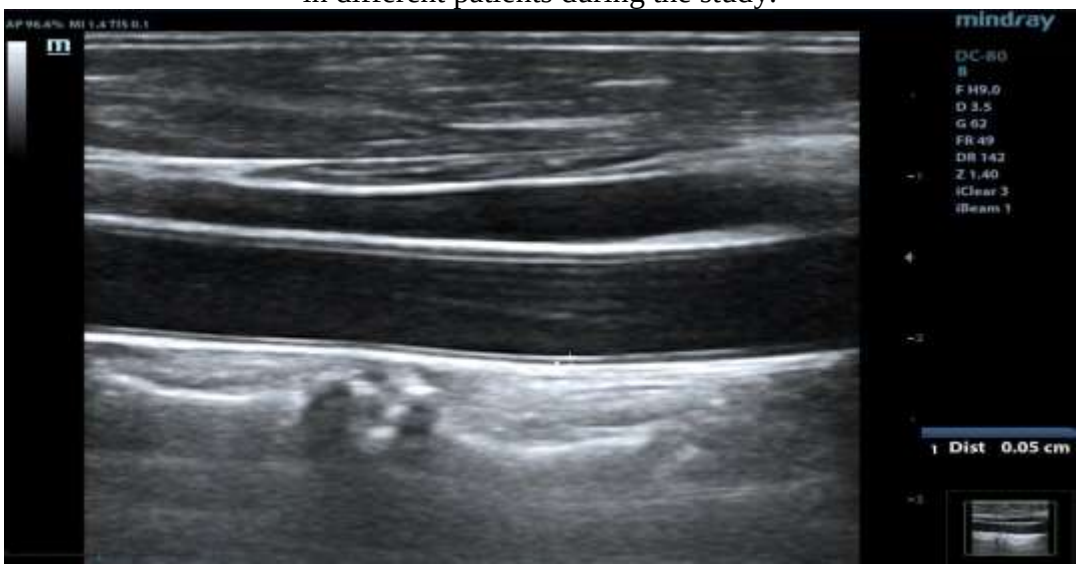

Fig.1: Normal IMT in left common carotid artery

Fig.2: Increased IMT in left common carotid artery

5. DISCUSSION

Cardiovascular disease is one of the most common causes of mortality and morbidity in diabetic patients. In the present study, we made an attempt to sonographically measure the CIMT in diabetic patients and found its association with traditional cardiovascular risk factors in type 2 diabetic patients.

Momeni *et al.)* [14]in their study reported the mean age of patients to be 59.65±9.37 years which is slightly higher than that in the present study where the mean age of patients was 54.57±10.66 years, however, in their study females (64.3%) outnumbered the males (35.7%) whereas in our study the proportion of males and females were equal. As far as other studies are concerned, the relationship of CIMT with traditional cardiovascular risk factors has been evaluated in a diversified age and sex profile of type 2 DM patients in different studies[13,15,16]. The age profile of the patients in the present study thus included both mature adults as well as elderly, thus addressing the most relevant group of patients at a risk of cardiovascular disease in a gender-balanced study population.

Dakre *et al.*[17] reported a dominance of those having a diabetic history >5 years (67%), however, they did not report the level of glycemic control in terms of HbA_{1c} or type of treatment. Omar *et al* [18]on the other hand, in the two study groups of their study reported the mean HbA_{1c} as 9.2 and 8% respectively, while in our study the mean HbA_{1c} was found to be 7.26±1.43%, however they also did not report the duration of diabetes and type of diabetic treatment availed which has been included in our study.

In the study by Dakre *et al.*[17] as many as 88% patients were overweight and obese as per BMI criteria, while in our study 85.5% patients were obese as per waist circumference criteria and as per waist-hip ratio criteria, there were 35.5% obese patients. In their study hypertriglyceridemia and low HDL were reported in 85% and 75% patients respectively. While in our study, hypertriglyceridemia and low HDL were seen in 59.1% and 60% patients which is comparatively lower. However, they did not report the status of other traditional cardiovascular risk factors, but in our study we have measured the mean blood pressure and behavioral risk factors like smoking and alcohol. As far as overweight/obesity was

concerned, the profile of their study was similar to that obesity profile of patients in the present study.

In the present study, mean carotid intima media thickness was observed to be 0.81±0.22 mm (0.80±0.21 mm for right and 0.82±0.23 mm for left sides respectively). As many as 46 (41.8%) patients had CIMT >0.9 mm, which is similar to the study done by Momeni *et al*[14] who reported the mean CIMT value to be 0.84±0.18 mm, however, they did not describe it in categorical terms.

In another study, Bhinder and Kamble[19] reported the mean CIMT to be 0.78±0.06 mm for both the right and left sides in prediabetic patients. Slightly higher mean CIMT in the present study could be attributed to the difference in diabetic status of the patients. Dakre *et al.*[17] on the other hand found majority of their patients (53%) with CIMT >0.9 mm which is similar to our study.

One of the limitations of the present study was absence of a control group owing to which it is difficult to comment on the relative increase in risk of CIMT abnormality in type 2 DM patients as compared to a non-diabetic population.

6. CONCLUSION

A significant association of abnormal CIMT was seen with different cardiovascular risk factors like older age, male sex, longer duration of diabetes, diabetic medication (OHA+insulin), poor glycemic control, larger waist hip ratio, central obesity as per waist circumference, smoking habit, hypertensive status and higher mean systolic and diastolic blood pressures and dyslipidemia. Abnormal CIMT in low risk population may alert the clinician early enough to intervene in order to prevent major cardio vascular/ cerebrovascular catastrophes.

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