Carotid Artery Intima Media Thickness in Predicting Coronary Artery Disease in Type II Diabetes Mellitus

Vevek Rana¹, Amit Johari², Meenakshi Sidhar³

^{1,2}Senior Specialist, Medicine Dept., Dr Baba Saheb Ambedkar Hospital & Medical College, Rohini, Delhi.

³HOD Blood Bank, Department of Pathology & Blood Bank, Dr Baba Saheb Ambedkar Hospital & Medical College, Rohini, Delhi.

DOI: <https://doi.org/10.24321/2349.7181.201812>

Abstract

Diabetes Mellitus is a chronic, common metabolic disorder characterised by high blood sugar levels over a prolonged period. Atherosclerosis involving the coronary, cerebral and peripheral (lower extremity) arteries is the predominant cause of diabetes related mortality, responsible for up to 70% of all deaths in patients with this disease.

Coronary angiography (CAG) has been considered as the gold standard for the assessment of the degree of Coronary atherosclerosis but measurement of carotid intima thickness by ultrasonography is a non invasive and quantitative method of evaluating early atherosclerosis. The aim of this study was to assess carotid artery intima media thickness and to assess any correlation between carotid artery intimal thickness and coronary artery disease in Type II DM.

This study was carried out in the department of medicine, Dr. Baba saheb Ambedkar hospital, Delhi to assess carotid intima media thickness (CIMT) as a risk factor for CAD in type II diabetes using Ultrasound B scan to assess CIMT.

In this study, 30 patients of DM type II with CAD, 30 patients of DM type II without CAD & 30 patients were age and sex matched controls who did not have any disease.

Mean CIMT was found to be significantly increased in DM type 2 with CAD group as compared to DM type 2 without CAD and the difference was found to be statistically significant ($P < 0.001$). Also the mean CIMT was significantly increased in DM type 2 with and without CAD as compared to controls and the difference was statistically significant.

Also, patients with more than 3 cardiovascular risk factors had significantly greater CIMT than patients who had less than 3 cardiovascular risk factors and the difference was statistically significant.

Keywords: Coronary Artery Disease (CAD), Diabetes Mellitus Type II, Coronary Atherosclerosis, Carotid Artery Intima Media Thickness (CIMT)

Corresponding Author: Dr. Amit Johari, Medicine Dept., Dr Baba Saheb Ambedkar Hospital & Medical College, Rohini, Delhi.

E-mail Id: dramitjohari@gmail.com

Orcid Id: <https://orcid.org/0000-0002-4651-6112>

How to cite this article: Rana V, Johari A, Sidhar M. Carotid Artery Intima Media Thickness in Predicting Coronary Artery Disease in Type II Diabetes Mellitus. *J Adv Res Med* 2018; 5(3): 1-6.

Introduction

Globally 422 million adults are living with diabetes according to latest 2016 WHO study. There were over 72 million cases of diabetes in India in 2017 (prevalence of 8.8%). There are two types of diabetes, Type 1 & Type 2. Type 1 diabetes is an autoimmune disease with a strong genetic component and can occur at any age, but tends to develop in childhood. Type 1 diabetes is characterised by destruction of pancreatic beta cells, culminating in absolute insulin deficiency. Type 1 diabetes (Insulin dependent) accounts for 5-10% of total cases of diabetes and Type 2 diabetes (non insulin dependent) account for 90-95% of total cases of diabetes. Cardiovascular diseases are increased both in individuals with type 1 or type 2 diabetes.

The Framingham Heart study revealed a marked increase in peripheral arterial disease, CHF, CAD, MI and sudden death (risk is increased from one to five fold) in DM. The American Heart association has designated DM as a major risk factor for cardiovascular disease.

Insufficient insulin effect plays a primary role in the metabolic derangements linked to diabetes; hyperglycaemia in turn plays an important role in disease related complications. Atherosclerosis involving the coronary, cerebral and peripheral (lower extremity) arteries is the predominant cause of diabetes related mortality, responsible for up to 70% of all deaths in patients with this disease.

Multiple metabolic disturbances may promote atherogenesis and predispose the patient to CAD/ischaemic stroke. These include reduced concentrations of HDL cholesterol; increased small dense LDL, and insulin resistance.

Coronary angiography (CAG) has been considered as the gold standard for the assessment of the degree of Coronary atherosclerosis, but angiographic assessment of the coronary arteries is expensive, needs expertise and tertiary care hospitals, and is not without risks. Since atherosclerosis is a generalised phenomenon and is more or less present equally in the coronary, cerebral and carotid arteries, so ultrasonographic assessment of easily accessible arteries such as carotid artery can provide information on intima media thickness, plaque presence, type of calcification and wall diameter which can enable examination of presymptomatic lesions, assess atherosclerosis burden and hence the risk of cardiovascular events.

Measurement of carotid intima thickness by ultrasonography is a non invasive and quantitative method of evaluating early atherosclerotic changes. It has been found in studies that diabetic patients have greater carotid intima media thickness as compared to non diabetics (Scott R Votey et al¹).

There are few Indian studies in which carotid intima media

thickness has been measured in type II diabetes Mellitus. The aim of this study was to assess intima media thickness of carotid artery and to assess any correlation between carotid artery intima media thickness and coronary artery disease in Type II DM.

Material and Methods

This study was carried out in the department of medicine, Dr. Baba saheb ambedkar hospital, Delhi to assess carotid intima media thickness (CMT) as a risk factor for CAD in type II DM. The sample size was 90 patients and these patients, who fulfilled the inclusion & exclusion criteria, were randomly selected from medicine OPD and wards and divided in three different groups of 30 each. First group was patients of DM type II with CAD, second group comprised of patients of DM type II without coronary artery disease and third group was controls without any disease. Patients who were more than 35 years of age and gave consent for study were included in the study. Patients less than 35 years of age or with history of congestive heart failure, renal disease, thyroid disease, hepatic disease, stroke, or rheumatoid diseases were excluded from this study.

Multistage random sampling was used in this study. All patients were taken after informed consent. A detailed history and physical examination was recorded including brachial blood pressure, height, weight, body mass index and waist hip ratio. History of hypertension, diabetes mellitus, chronic kidney disease and dyslipidemia was noted.

The patients were subjected to various laboratory tests including fasting and post prandial (2hrs) blood sugar, kidney function tests, liver function tests, thyroid function tests, lipid profile, glycated hemoglobin, urine routine and microscopy.

Presence of hypertension was defined as per the Joint national committee (JNC) criteria. Presence of diabetes was defined by American Diabetes Association criteria. Smoking status was recorded as number of pack years smoked. Dyslipidemia was diagnosed based on ATP III guidelines (JAMA 2001).

BMI was calculated by Quetlet index. $BMI = \frac{\text{weight in kg}}{\text{Height in meters}^2}$

BMI <18.5 is underweight, 18.5-24.9 is normal, 25-29.9 is overweight and 30-39.9 is obese.

Ultrasonographic scanning of carotid arteries was performed on Toshiba zario machine equipped with colour flow imaging and pulse Doppler with an electrical linear transducer of frequency between 5-12 megahertz.

Scanning of the extra cranial carotid arteries in the neck

was performed bilaterally in the supine position with the neck extended in three different longitudinal projections (i.e. anterior oblique, lateral and posterior-oblique) and in the transverse projection. This method allowed the common carotid artery, the carotid bulb, and the internal and external carotid artery to be scanned. The carotid vessels were followed from the clavicular head cephalad to their bifurcation and 3-4 cm of the proximal internal and external carotid arteries were studied. The CIMT was measured about 15 mm proximal to the carotid bulb bilaterally and the average was taken of the CIMT value of both right and left common carotid arteries. The scanning sessions were for an average 20 mins. Carotid CIMT was defined as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line on the scans, with the first line representing the lumen intimal interface and the second line representing the collagen containing upper layer of adventitia. In each longitudinal projection, the site with the greatest thickness (including plaque) was detected along the vessel from the common carotid artery to the internal carotid artery. Four measurements of the IMT were made at the site of greatest thickness by visual examination and at two other points (1cm proximal and 1cm distal to the site). These four measurements were averaged. The greatest value among the eight averaged IMTs (four from right side and four from left side) was used as the representative value (the absolute value in mm of IMT) for each individual. IMT below 0.8 mm is considered normal. The presence of plaque & degree of stenosis was noted and analysed. Plaque is defined as localised lesion of thickness >1.0mm; stenosis as 50% occlusion with systolic frequency peak >4.0 KHZ and spectral broadening.

Results

In this study, 30 patients of DM type II with CAD, 30 patients of DM type II without CAD & 30 patients were age and sex matched controls who did not have any disease (Table 1 & Figure 1).

Table 1

Age (Years)	DM with CAD	DM without CAD	Control
35-44	3	1	2
45-54	7	8	7
55-64	11	12	11
65-74	9	9	10
Total	30	30	30

Figure 1

- Majority of patients of DM type II with CAD belonged to age group 55-64 years (n=11) & 65-74 years (n=9).
- Mean age of these cases was 57.2 years.
- Majority of patients of DM type 2 without CAD belonged to age group of 55-64 years (n=12) & 65-74 years (n=9).
- Mean age of these cases was 58.9 years.

Table 2

Symptoms	DM with CAD	%
Chest Pain	17	56.67
Dyspnea	4	13.33
Syncope	2	6.67
Palpitation	1	3.33
Epigastric Pain	1	3.33
Chest pain+Dyspnea	4	13.33
Chest pain+Palpitation	1	3.33
Total	30	100

In the case group, most common presenting symptom was chest pain (n=17) in 56.67%, followed by dyspnea (n=4) in 13.3%, chest pain with dyspnea (n=4) in 13.33%.

Table 3

Risk Factors	DM with CAD (n=30)	%	DM without CAD (n=30)	%	(n=30) controls	%
Alcohol	19	63.35	11	36.67	5	16.67
Smoking	20	66.67	13	43.33	4	13.67
Hypertension	19	63.33	18	60	0	0.00
Hyperlipidemia	20	66.67	14	46.67	3	10
Family H/ o CAD	6	20	5	17.67	2	16.67

Distribution of risk factors in cases & controls is shown in Table III. In 30 cases of DM type 2 with CAD, alcohol intake was found in 19 cases, smoking in 20 cases, hypertension in 19 cases, hyperlipidemia in 20 cases and family h/o CAD in 6 cases (Table 3).

Table 4

BMI (kg/m)	DM with CAD	DM without CAD	Controls
18.5-24.9	6	5	25
25-29.9	18	19	5
>30	6	6	0
	30	30	30

In DM type 2 with CAD group, 24 (80%) patients were overweight.

In DM type 2 without CAD group, 25 patients (83.33%) were overweight.

In control group, only 5 subjects were overweight.

BMI between DM type 2 with CAD & without CAD did not show any statistically significant difference in the present study.

Table 5

DM with CAD	DM without CAD	Controls
1.13 ± 0.29 mm	0.73 ± 0.20 mm	0.57 ± 0.12 mm

P value between

DM with CAD & Controls P value <0.001	DM without CAD & Controls P value <0.05	DM with CAD & DM without CAD group P value <0.001
--	--	--

In DM type 2 with CAD group, majority of patients, 28 out of 30 patients had carotid intima media thickness above 0.8 mm, whereas in DM type 2 without CAD, only 10 out of 30 patients had carotid intima media thickness above 0.8 mm. In control group, only 2 out of 30 patients had Carotid intima media thickness above 0.8 mm (Table 4).

Mean CIMT was significantly increased in DM type 2 with CAD group compared to DM type 2 without CAD and the difference was statistically significant ($P < 0.001$). Also the mean CIMT was significantly increased in DM type 2 with and without CAD as compared to controls and the difference was statistically significant (Table 5).

Also, patients with more than 3 cardiovascular risk factors had significantly greater CIMT than patients who had less than 3 cardiovascular risk factors and the difference was statistically significant.

Table 6

	DM with CAD	DM without CAD	Controls
CIMT (Mean)	1.1267 ± 0.30 mm	0.73 ± 0.20 mm	0.596 ± 0.19 mm
Plaque Occurrence	12 (40%)	26 (6.66%)	0(0%)

One or more plaque was seen in carotid artery in about 40% of patients of DM type 2 with CAD group while only 6.66% patients of DM type 2 without CAD had plaques in their carotid arteries. Also no subject in control group had plaques in their carotid arteries. Positive predictive value for diagnosis of CAD with plaque occurrence is 85% (Table 6).

6 out of 30 patients in diabetes Mellitus type 2 with CAD had more than 50% carotid artery stenosis, whereas only 1 out of 30 patients in DM type 2 without CAD group had more than 50% carotid artery stenosis.

Discussion

Coronary artery disease (CAD) is a major cause of morbidity and mortality in developed world, and the incidence is also rising in developing world too. Atherosclerosis is a major cause of CAD and atherosclerosis can be detected and documented in early stages by examining intima media thickness (IMT) of peripheral arteries, especially carotid artery. IMT is measured by B mode ultrasound. Ultrasound scanning of carotid IMT is shown to be of clinical value in the screening of patients with CAD in various other published studies.

The findings of our study show that increase in CIMT is associated with the presence and extent of CAD. Coscun U et al² also found in their study that Carotid Doppler ultrasonography can be utilized as a valuable screening tool due to its several advantages, including ease of application, reproducibility, low cost and strong correlation with atherosclerosis.

In our study, Out of 30 patients with DM type 2 with CAD, 28 patients had CIMT > 0.8 mm which was taken as significant IMT based on previous studies. Among 30 patients with DM type 2 without CAD, only 10 had IMT > 0.8 mm and in control subjects, only 2 had IMT > 0.8 mm. On applying Chi-square test, the odds ratio, (95% CI) between DM type 2 with and without CAD is 0.12. P value is highly significant

($p < 0.001$). This means IMT was significantly increased in diabetic patients who had CAD as compared to diabetic patients without CAD.

The mean CIMT in patients with DM type 2 with CAD was 1.13 ± 0.29 mm, while in patients with DM type 2 without CAD was 0.73 ± 0.20 mm and in control group it was 0.57 ± 0.12 mm. Mean CIMT is significantly increased in DM type 2 with CAD and this difference is statistically significant (P value < 0.01).

Agarwal et al³ found a higher CIMT in diabetics who had CAD, even when the CAD was not clinically overt, leading to the conclusion that CIMT is a reliable surrogate marker for subclinical CAD in diabetic patients.

In the present study, we found that mean CIMT in patients with 0-2 cardiovascular risk factors was 0.994 ± 0.135 .

Mean IMT in patients with > 3 cardiovascular risk factors is 1.400 ± 0.279 .

The difference between these two groups is statistically significant and it means that more the number of risk factors, more is the risk of development of atherosclerosis and its complications. Kablak, Ziembicka et al⁴ demonstrated that hypertension, hyperlipidemia and DM are related to greater CIMT

Kota SK et al⁵ also concluded in their study that CIMT can be used as a valuable routine screening tool for the evaluation of atherosclerosis in T2DM patients in their study on CIMT Type 2 DM patients with ischaemic stroke.

Positive predictive value for diagnosis of CAD with plaque occurrence was found to be 85% in our study. One or more plaque was seen in carotid artery in about 40% of patients of DM type 2 with CAD group while only 6.66% patients of DM type 2 without CAD had plaques in their carotid arteries.

Chang CC et al⁶ findings also suggested in their study that carotid plaques are a strong predictor of stable CAD.

Limbu YR et al⁷ also reported increased CIMT and presence of soft carotid plaques in the majority of young Nepalese patients with documented CAD. The majority of carotid plaques were detected at carotid bulbs.

Also, Increased CIMT correlated with evidence of angiographically proven CAD in the study by Holland Z et al⁸.

Conclusion

The present study demonstrated the usefulness of carotid IMT as marker of atherosclerosis, which is strongly associated with standard risk factors. It can be used as a surrogate marker in prediction of coronary artery disease. Carotid B mode ultrasound is safe, non-invasive procedure for detecting clinical and preclinical coronary artery disease. Routine carotid ultrasound in Type 2 DM population may be worthwhile for the early detection and prevention of CAD but more large scale studies are required to establish its role in clinical practice.

Conflict of Interest: None

References

1. Scott R Votey, MD, Anney L Peters, Endocrine and Metabolic Diabetes Mellitus, Type 2, A review updated, Sep 23 2010.
2. Coskun U Yildiz A Email author, Ozlem B Esen, Baskurt M, A Cakar M, Kadriye O Kilickesmez, Lutfu A Orhan and Seyma Yildiz, A Relationship between carotid intima-media thickness and coronary angiographic findings: a prospective study. *Cardiovascular Ultrasound* 2009; 7:59.
3. Agarwal AK, Gupta PK, Singla S, Garg U, Prasad A, Yadav R. Carotid intimal-medial thickness in type 2 diabetes patients and its correlation with coronary risk factors. *J Assoc Physicians India* 2008;56:587–90. [PubMed].
4. Kablak-Ziembicka A Przewlocki T, Tracz W, Pieniazek P, Musialek P, Sokolowski A. Gender differences in carotid intima-media thickness in patients with suspected coronary artery disease. *Am J Cardiol* 2005;96(9):1217–1222.
5. Sunil Kumar Kota, Girija Ballav Mahapatra, [...], and Kirtikumar D. Modi Carotid intima media thickness in type 2 diabetes mellitus with ischemic stroke *Indian J Endocrinol Metab* 2013 Jul-Aug; 17(4): 716–722.
6. Chao-Chien Chang, Mei-Ling Chang, [...], and Chih-Hui Chin Carotid intima-media thickness and plaque occurrence in predicting stable angiographic coronary artery Clin Interv Aging. 2013; 8: 1283–1288.
7. Limbu YR, Rajbhandari R, Sharma R, et al. Carotid intima-media thickness (CIMT) and carotid plaques in young Nepalese patients with angiographically documented coronary artery disease. *Cardiovascular Diagnosis and Therapy* 2015;5(1):1-7. doi:10.3978/j.issn.2223-3652.2015.01.10.
8. Holland Z, Ntyintyane L, Gill G, Raal F. Cardiovasc J Afr, Carotid intima-media thickness is a predictor of coronary artery disease in South African black patients. 2009 Jul.

Date of Submission: 2018-04-25

Date of Acceptance: 2018-05-01