ORIGINAL RESEARCH

Assessment of Carotid Artery Intima Media Thickness and Its Correlation to Atherosclerotic Risk Factors in Type 2 Diabetes Mellitus: An Observational Study

[1]Dr. Aditi Rajan, [2]Dr. Anurag Prasad, [3]Dr. A K Agarwal, [4]Dr. V P S Punia, [5]Dr. Ajoy Deshmukh

[1]Post graduate, [2,4,5]Professor, [3]Professor & Head of the Department, School Of Medical Sciences & Research, Sharda University, India
[6]Assistant Professor, Department of Radiology, School Of Medical Sciences & Research, Sharda University, India

Corresponding author
Dr. Aditi Rajan
Post graduate, Department of Medicine, School Of Medical Sciences & Research, Sharda University, India

Received: 07 June, 2023 Accepted: 11 July, 2023

ABSTRACT

Background: One of the important causes of mortality in diabetes mellitus (DM) is cardiovascular diseases. Carotid artery intima media thickness (CIMT) is endorsed by the American Heart Association as being safe, non-invasive and less costly method of evaluating sub-clinical atherosclerosis. The main aim was to assess CIMT and its correlation with atherosclerotic risk factors in type 2 DM. **Methods:** The study was conducted on 100 patients who were adults of >30 years of either gender with diagnosed type 2 diabetes mellitus, admitted in the in-patient department. CIMT was measured with Philips Epiq 7G ultrasound machine having high frequency (3 to 12 MHz) linear transducer. **Results:** Mean age of enrolled patients was 57.41+8.1 years, 62% being males. 17 patients were found to have atheroembolic disease. Mean CIMT was found to be 0.72+0.21 mm. 30 patients were found to have high CIMT (>0.9 mm). Mean body mass index and mean waist circumference were significantly greater in the high-CIMT group (p<0.05).Mean HbA1c as well as mean post-prandial blood sugar were significantly higher in high-CIMT subgroup (p<0.05).The mean creatinine and lipid parameters were also significantly higher in the high-CIMT group (p<0.05).43.33% patients in high-CIMT group and only 5.71% patients in low-CIMT had athero-embolic evidence. **Conclusion:** Large number of type 2 DM patients had high CIMT. Additionally, patients with high CIMT were found to have significantly greater presence of atherosclerotic risk factors, indicating that CIMT is a strong indicator for atherosclerosis.

Keywords: Carotid artery intima media thickness, type 2 diabetes mellitus, atherosclerosis

INTRODUCTION

Diabetes mellitus (DM) is a major global health concern, affecting lakhs of people worldwide. According to the data released by WHO, the number of diabetic patients has surged from 108 million in 1980 to an astounding 422 million in 2014. In 2016, an estimated 1.6 million deaths were directly caused by diabetes. Another 2.2 million deaths were attributable to high blood glucose in 2012.[1] Majority of these cases are type 2 DM (91%), according to the International Diabetes Federation (IDF).[2] About 3/4th of the DM patients globally belongs to the low-income and middle-income nations like India.[3] It is projected that in the year 2015, India had more than 6.9 crore DM patients, which is the second highest number in the world after China.[2] The DM prevalence is predicted to double after 2 decades, because of the rising age-expectancy, high obesity prevalence along with higher exposure of population to various types of risk factors. One of the important causes as to why diabetic patients have a 2–4 times higher mortality because of cardiovascular causes as compared to normal population is the development of premature as well as severe atherosclerosis.[4] Cerebrovascular complications are also common in DM patients, with the risk of stroke increasing to around four times in these patients. Thus, diagnosis and treatment of the numerous complications of DM, particularly the macrovascular complications such as coronary artery disease and cerebrovascular disease, is an important part of managing DM. Hence, it can be safely said that atherosclerosis risk and type 2 DM go together.

Coronary as well as cerebral angiography have been deemed as the gold standard for the evaluation of the degree of coronary atherosclerosis. But angiographic evaluation of the coronary arteries is costly, needs tertiary care hospitals as well as technical expertise and is not without the risks involved. It is vital to keep in mind that atherosclerosis is a widespread phenomenon and is present similarly in the coronary, carotid, and cerebral arteries. Therefore, ultrasonographic measurement of carotid arterial wall thickness is a helpful non-invasive tool to assess the extent of atherosclerosis. This methodrelates well with histological examination of the carotid arteries.[5] Measurement of only the intima media thickness of the common carotid arteries, in contrast to a more comprehensive carotid Doppler study, is a dependable method to identify the atherosclerosis severity.[6] These findings can also be related to systemic generalized atherosclerosis.[7] The carotid artery intima media thickness (CIMT) can be assessed with a high level of accuracy and reproducibility with the help of B mode ultrasonography that provides a dependable and legitimate estimate of the arterial wall thickness.[8] In scientific literature, CIMT in healthy normal middle-aged adults has been defined as 0.6–0.7 mm and a thickness of more than 1.2 mm is deemed to be a plaque.[9] According to study by Van Der Meer et al, CIMT rise in participants over a period of 6.5 years was linked to male gender, body mass index (BMI), smoking, increasing age, and hypertension while no connection was observed with dyslipidemia.[10] However, if we discuss about the related scientific evidence from India, they are scarce. A study conducted by Agarwal et al. in 2009 found that CIMT is associated with various atherogenic risk factors like diabetes mellitus, dyslipidemia, hypertension, and smoking.[11] Another study published in 2012 by Gayathri et al. concluded that CIMT is significantly greater in those type 2 DM patients who suffered from atherosclerotic events than in those type 2 DM patients who had only risk factors for atherosclerosis but did not suffer from any events.[12]

Considering the increasing prevalence of atherosclerotic events, it is important to generate more evidence related to the predictive utility of non-invasive investigations like CIMT measurement. This may help in early alerting of the clinician with regards to the cardiovascular event risk, leading to quicker interventions. Hence, it was decided to evaluate the CIMT & it's correlation to atherosclerotic risk factors in type 2 DM patients, at a tertiary care teaching hospital. This was conducted to create more evidence with regards to assessment of the predictive value of CIMT as an early indicator of atherosclerosis in the DM cases.

METHODS

This was a prospective, observational study conducted between **1st January 2019 to 30th June 2020**. The study was initiated after getting permission from the institutional ethics committee. Inclusion criteria comprised of adult patients of age more than 30 years, of either gender with diagnosed type 2 DM, admitted in the in-patient department (IPD) at School of Medical sciences & Research, Sharda University. The exclusion criteria comprised of type 1 DM patients, patients with cardioembolic stroke, hemorrhagic stroke & stroke due to secondary causes like trauma, impaired coagulation or tumor. Patients who had history of secondary diabetes, congestive cardiac failure, overt renal failure, urinary tract infection or recent intercurrent illnesses were also excluded. Only the patients who fulfilled all the screening criteria were included, only after the patients signed the informed consent document.

The criteria used for diagnosing and/or confirming type 2 diabetes mellitus was as follows:

- Fasting plasma glucose ≥ 126mg/dl, or
- 2 hour postprandial/OGTT plasma glucose ≥ 200mg/dl as per the latest ADA guidelines.

After enrollment of the patients in the study, demographic details like age and gender were noted down. Detailed history and physical examination were recorded, which included assessment of anthropometric measurements like weigh, height, body mass index (BMI) and the waist circumference. For measuring waist circumference, a point at the highest point of iliac crest crossing the mid axillary line on the right side of the trunk was taken and the circumference was measured horizontally at normal minimal respiration. Hip circumference was measured at the widest point between the hip and buttocks. Waist hip ratio (W/H), defined as waist circumference divided by hip circumference, was noted down. Routine blood investigation was also conducted to evaluate complete blood count, lipid profile, HbA1c, renal as well as liver function tests.

Carotid artery intima media thickness was measured with the help of Philips Epiq 7G ultrasound machine with a high frequency (3 to 12 MHz) linear transducer was used. Scans were completed 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 6 mm of common carotid, the carotid bulb as well as the proximal 6 mm of internal carotid artery of both sides. The final CIMT considered was the average of the IMT values at the various sites examined.

After data collection, data entry was done in a Microsoft Excel sheet. Data analysis was done with the help of statistical software Graphpad InStat.v3.0 (USA). Quantitative data, viz. the anthropometry details, blood parameters and CIMT details were presented with the help of Mean and Standard deviation. Descriptive statistics were used to note down the distribution of patients based on age, gender, patient history details. The patients were also classified into two groups depending on a defined cut-off for CIMT (<0.9 and >0.9). The relevant continuous parameters were compared between the two sub-groups using unpaired t test. The parameters like comorbidities (hypertension), BMI status, waist-hip ratio status was associated with the CIMT status (>0.9 and <0.9) using chi-square test. P value of less than 0.05 was considered significant.

RESULTS

A total of 100 patients were enrolled in the study. The mean age of the patients in the study was found to be 57.41 + 8.1 years, with a range of 38 years to 76 years. 62% of the enrolled patients were males. The mean BMI of the patients was found to be 29.39 + 1.75 kg/m2, while the mean waist circumference of the patients was found to be 98.94 + 6.88 cm (Table 1). 39% of the patients in the study was found to be between 51-60 years while 37% of the patients were found to be between 61-70 years. 19% of the patients were found to be between 41-50 years, while only 3 patients were below 40 years of age (Figure 1)

On assessing the details of diabetes mellitus in study participants, the mean years of diabetes duration since diagnosis was found to be 6.46 years. The baseline mean fasting blood sugar was calculated to be 149.02 + 33.98 mg/dl while the baseline mean post-prandial blood glucose was calculated to be 230.99 + 64.3 mg/dl. The mean baseline HbA1c was also calculated to be 10.96 + 2.31 g% (Table 2). 49% patients had diabetes from duration of 1-5 years, while 41% patients had diabetes from a duration of 6-10 years (Figure 2).

The number of patients with hypertension in the study was found to be 66. The overall mean systolic blood pressure was calculated to be 146.75 + 14.72 mm Hg while the mean diastolic pressure was found to be 92.84 + 8.64 mm Hg (Table 3).

The mean hemoglobin was calculated to be 13.88 + 0.95 g/dl while the mean total WBC count was calculated to be 8327.1 + 7537.36 / mm3. The renal function test assessment showed mean urea to be 32.5 + 9.16 mg/dl while the mean creatinine to be 1.04 + 0.31 mg/dl. On assessing the lipid profile of the patients, mean total cholesterol was found to be 210.21 + 45.05 mg/dl, mean triglyceride to be 162.1 + 26.78 mg/dl, mean HDL was 38.74 + 5.65 mg/dl while mean LDL was calculated to be 128.63 + 32.74 mg/dl (Table 4). On assessing any evidence or history of atheroembolic disease, 17 patients were found to have atheroembolic disease while remaining 83 patients did not have history or evidence of atheroembolic disease.

The mean CIMT on the right side was calculated to be 0.7 + 0.23 mm, while the mean CIMT on the left side was found to be 0.73 + 0.23 mm. The mean CIMT was calculated for each patient first (right + left/2) and then overall mean of the patients was assessed. The overall mean CIMT was calculated to be 0.72 + 0.21 mm. The number of patients with CIMT >0.9 mm was found to be 30, indicating higher than normal values. The remaining 70 patients had CIMT below 0.9 mm (Table 5).

The high CIMT (>0.9 mm) and low CIMT (<0.9 mm) patient subgroups were compared. It was found that mean BMI was significantly higher in the high-CIMT group (p<0.05) while the mean waist circumference was also found to be significantly greater in the high-CIMT group (p<0.05). The mean age and gender distribution were statistically comparable in both the sub-groups (p>0.05) (Table 6).

The proportion of hypertensive patients in the low-CIMT (65.72%) and high CIMT groups (66.67%) were found to be statistically comparable (p>0.05) (Table 7).On comparing the mean SBP and the mean DBP between the two study sub-groups, no significant difference was found between the low-CIMT and high-CIMT sub-groups (p>0.05) which indicates that the blood pressure was comparable (Table 8).

On comparing the diabetes parameters between the two sub-groups, the mean HbA1c as well as mean PPBS was found to be significantly higher in the high-CIMT group (p<0.05). The mean duration of DM was numerically greater in the high-CIMT group, but statistically comparable (p>0.05). The mean FBS was also found to be comparable in the two sub-groups (p>0.05) (Table 9).

The mean hemoglobin as well as the mean TLC were found to be comparable between the two sub-groups. The mean urea was numerically higher in the high-CIMT group but statistically comparable (p>0.05). The mean creatinine was significantly higher in the high-CIMT group as compared to low-CIMT (P<0.05). The lipid profile was significantly worse in high-CIMT group, with mean total cholesterol, mean triglyceride as well as mean LDL all being significantly higher in the high CIMT group (p<0.05) (Table 10).

On assessing the association between evidence of atheroembolic disease and high CIMT, 43.33% of patients in the high-CIMT group had atheroembolic evidence while only 5.71% of patients in low-CIMT had atheroembolic evidence. This difference between the two study sub-groups was found to be statistically significant (p<0.05) (Table 11).

Table 1: Demographic details of enrolled patients in study (n=100)

Parameter assessed	Calculated value
Mean age (years)	57.41 + 8.1
Median age (years)	57.5
Age range (years)	38-76
Number of males	62
Number of females	38

Mean body mass index (BMI) (kg/m2)	29.39 + 1.75
Mean waist circumference (cm)	98.94 + 6.88

Table 2: Diabetes mellitus related findings in the study

Parameter assessed	Calculated value
Mean years of disease	6.46 + 3.61
Mean Fasting blood glucose (mg/dl)	149.02 + 33.98
Mean post-prandial blood glucose (mg/dl)	230.99 + 64.3
Mean HbA1c (g%)	10.96 + 2.31

Table 3: Blood pressure related findings in the study

Parameter assessed	Calculated value
Mean systolic blood pressure (mm Hg)	146.75 + 14.72
Mean diastolic blood pressure (mm Hg)	92.84 + 8.64
Number of patients with Hypertension	66
Number of patients without Hypertension	34

Table 4: Blood count parameters of patients in the study

Parameter assessed	Calculated value
Routine blood count	
Mean hemoglobin (g/dl)	13.88 + 0.95
Mean total leukocyte count (TLC) (per mm3)	8327.1 + 7537.36
Renal function test	
Mean urea (mg/dl)	32.5 + 9.16
Mean creatinine (mg/dl)	1.04 + 0.31
Lipid profile	
Mean total cholesterol (mg/dl)	210.21 + 45.05
Mean triglyceride (mg/dl)	162.1 + 26.78
Mean HDL (mg/dl)	38.74 + 5.65
Mean LDL (mg/dl)	128.63 + 32.74

Table 5: Carotid intima media thickness (CIMT) findings in the study

Parameter assessed	Calculated value
Mean right CIMT (mm)	0.7 + 0.23
Mean left CIMT (mm)	0.73 + 0.23
Mean average CIMT (mm)	0.72 + 0.21
Number of patients with CIMT (< 0.9 mm)	70
Number of patients with CIMT (> 0.9 mm)	30

Table 6: Comparison between demographic features of high CIMT and low CIMT groups

	Low CIMT (<0.9) (n=70)	High CIMT (>0.9) (n=30)	P value
Mean age	57.9 + 8.39	56.5 + 7.42	0.67
Mean BMI (kg/m^2)	27.89 + 1.61	31.55 + 1.52	**0.04***
Mean Waist circumference (cm)	96.35 + 6.9	103.6 + 5.3	**0.03***
Number of males	42 (60%)	20 (66.67%)	
Number of Females	28 (40%)	10 (33.33%)	0.53

Gender comparison done by Chi-square test, other parameters compared by unpaired t test, P<0.05 considered significant

Table 7: Association of Hypertension and increased CIMT thickness in study

	Low CIMT (<0.9) (n=70)	High CIMT (>0.9) (n=30)
Hypertensive patients	46 (65.72%)	20 (66.67%)
Non-hypertensive patients	24 (34.2%)	10 (33.33%)
P value	0.57 (Not significant)	

P value by Chi-square test considered not significant

Table 8: Comparison between blood pressure of high CIMT and low CIMT groups

	Low CIMT (<0.9) (n=70)	High CIMT (>0.9) (n=30)	P value
Mean SBP (mm Hg)	145.7 + 15.5	149.2 + 12.62	0.71

Mean DBP (mm Hg)	92.31 + 8.3	94.07 + 9.41	0.74

P >0.05 by unpaired t test, considered not significant

Table 9: Comparison between diabetes parameters of high CIMT and low CIMT groups

	Low CIMT (<0.9) (n=70)	High CIMT (>0.9) (n=30)	P value
Mean duration of DM	6.18 + 3.7	6.63 + 3.42	0.11
Mean HbA1c (g%)	9.78 + 2.28	11.39 + 2.33	**0.02***
Mean FBS (mg/dl)	149.1 + 34.62	148.3 + 33.02	0.79
Mean PPBS (mg/dl)	221.4 + 59.3	245.1 + 66.3	**0.04***

P >0.05 by unpaired t test, considered not significant

Table 10: Comparison between other blood parameters of high CIMT and low CIMT groups

	Low CIMT (<0.9) (n=70)	High CIMT (>0.9) (n=30)	P value
Mean hemoglobin (g/dl)	13.82 + 0.96	14.02 + 0.87	0.31
Mean total leukocyte count (TLC) (per mm3)	8532.11 + 1854.68	9082.3 + 2072	0.27
Renal function test			
Mean urea (mg/dl)	31.76 + 8.86	35.23 + 9.75	0.13
Mean creatinine (mg/dl)	1.01 + 0.29	1.11 + 0.35	**0.02***
Lipid profile			
Mean total cholesterol	201.59 + 41.3	230.3 + 47.66	**0.01***
Mean triglyceride (mg/dl)	156.76 + 23.93	174.2 + 30.59	**0.01***
Mean HDL (mg/dl)	38.82 + 5.41	38.53 + 6.29	0.82
Mean LDL (mg/dl)	123.1 + 27.45	142.5 + 40.25	**0.01***

P <0.05 considered significant by unpaired t test

Table 11: Association of evidence of atheroembolic disease and high CIMT

	Low CIMT (<0.9) (n=70)	High CIMT (>0.9) (n=30)
Atheroembolic evidence positive	4 (5.71%)	13 (43.33%)
Atheroembolic evidence negative	66 (94.29%)	17 (56.67%)
P value	**<0.01* (Significant)**	

P value by Chi-square test considered significant

Table 12: Demographic details in similar studies

Mean age in studies	
Our study	57.41 years
Gayathri et al.[12]	55.79 years
Kota et al.[21]	60.4 years
Okayama et al.[22]	59 years
Gender distribution in studies	
Our study	Males: 62%, Females: 38%
Butt et al.[23]	Males: 60%, Females: 40%
Gayathri et al.[12]	Males: 68%, Females: 32%
Kota et al.[21]	Males: 75%, Females: 25%
Okayama et al.[22]	Males: 57%, Females: 43%

Figure 1: Age distribution of patients in study

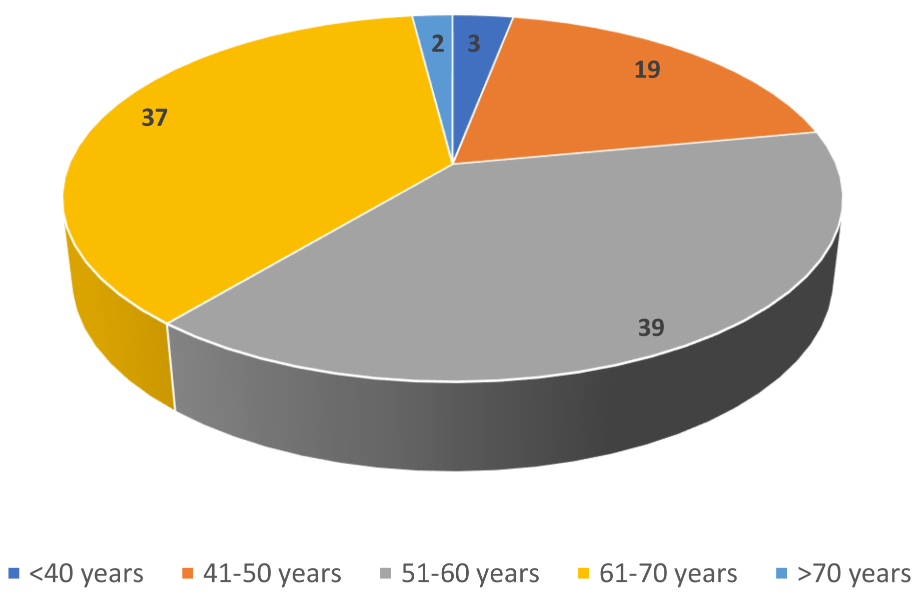
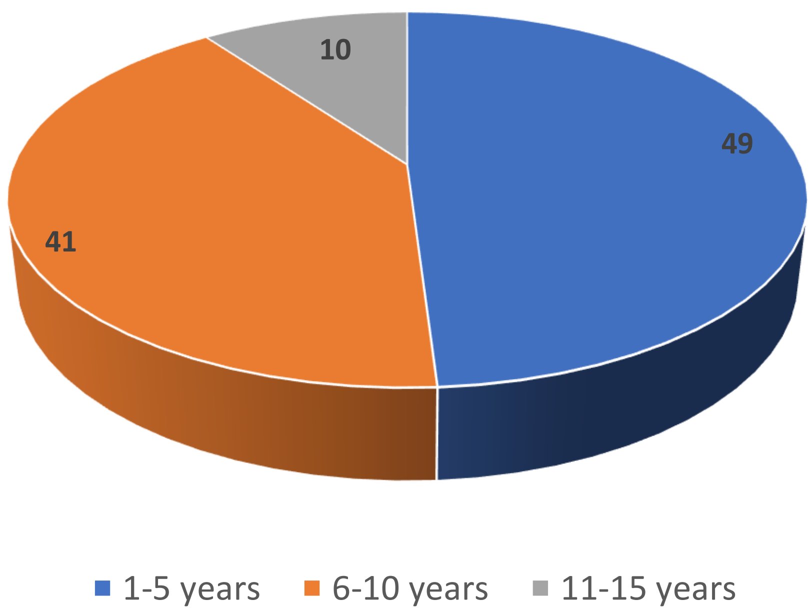


Figure 2: Duration of diabetes in study



DISCUSSION

Patients with type 2 diabetes mellitus (T2DM) are at elevated risk for acquiring cardiovascular diseases (CVD), that are one of the chief reasons of death in these class of patients.[13,14] Given that not all T2DM patients develop CVD, it is important to identify patients with great probability of suffering from these diseases. This early identification can help for efficient early intervention and treatment that could eventually reduce morbidity and mortality. The carotid intima-media thickness (CIMT) is a well-established non-interventional surrogate indicator for the likelihood of cardiovascular (CV) occurrences for the general population.[15] Previous studies revealed that basal IMT forecasted the occurrence of CV events in patients with T2DM.[16,17] Based on these outcomes, CIMT alterations calculated by repeated CIMT assessment are generally used as a surrogate indicator for intervention in multiple clinical studies. However, the relationship between changes in CIMT and the incidence of CV events has not yet been fully addressed. In recent times, it was revealed that CIMT advancement was related with the occurrence of stroke in patients not suffering from frequent CV events.[18] On the contrary, while the European Lacipidine Study on Atherosclerosis (ELSA) revealed a positive correlation between baseline CIMT and the stroke incidence, it did not show any relationship between CIMT alteration and the occurrence of stroke.[19]Additionally, a meta-analysis data also indicated that CIMT progression did not have any relationship with CV events in the general population.[20] Thus, it remains controversial whether changes in CIMT can predict CV events in contrast to baseline CIMT. Furthermore, there is also uncertainty about the usefulness of CIMT progression as a predictor of CV events in patients with T2DM. Hence, we decided to evaluate the relationship of CIMT with atherosclerotic risk factors in patients with T2DM. This will help in creating evidence which can help the physicians in classifying high-risk patients early on, so that necessary screening and monitoring for atherosclerosis can be done.

In the present study, the majority patients fell n the 51-60 years of age category, with the mean age also falling between the range (57.41 years). Majority of the enrolled patients were males (62%). Identical demographic trend was noted in other similar studies (Table 12).[12,21-23] Majority of the T2DM patients were found to be having hypertension as well (66%). This is a common phenomenon, and especially since most of the patients were of age more than 50 years, multiple comorbidities were not surprising. The complete blood count results were within normal range, but the kidney function tests revealed higher than normal mean urea (32.5 mg/dl) and serum creatinine also deranged in patients. This was again not surprising as older patients with T2DM are known to have deranged renal function tests because of associated diabetic nephropathy. The lipid profile of these patients was also found to be deranged, with the mean cholesterol (210.21 mg/dl) and mean triglyceride (162.1 mg/dl) being above the normal range.

On comparing the mean CIMT in the right and left side, no significant difference was found ($p>0.05$). The overall mean CIMT was found to be 0.72 + 0.21 mm. In the study by Butt et al., the mean CIMT on the right was 0.88 mm while on the left side was found to be 0.93 mm, which was found to be comparable as was the case in our study.[23] The overall mean CIMT was found to be 0.85 mm in the study by Kota et al.,[21] while it was found to be 0.84 mm in the study by Agarwal et al.[24] The lower mean CIMT in our study may be attributed to the fact that the patients were not newly diagnosed DM patients in our study, and were receiving medications from a long time, which may not be the case in other compared studies.

30% of the T2DM patients in present study were having a CIMT of greater than 0.9 mm. On assessing the available scientific literature, it was found that CIMT of less than 0.9 mm has been considered normal, while more than 0.9 mm has been considered of higher level. After subdivision of the patients based on CIMT, it was found that mean BMI as well as the mean waist circumference were significantly higher in the high-CIMT group ($p<0.05$). This indicates that obesity may be a factor which can be related to a higher CIMT in the T2DM patients. No significant association was found between high CIMT and hypertension, as both the sub-group of patients had similar hypertension prevalence. The mean SBP as well as DBP were found to be comparable in the sub-group of patients. On comparing the diabetes parameters, it was found that the mean duration, and mean FBS were comparable in both the sub-groups ($p>0.05$). However, the mean HbA1c as well as the mean PPBS were found to be significantly higher in the high-CIMT group ($p<0.05$). This indicates that uncontrolled diabetes mellitus may be one of the risk factors for increased CIMT in the patients. Macrovascular disease is the most crucial cause of mortality as well as morbidity in patients with type 2 diabetes. Even when adjusted for predictable risk factors, diabetic patients still show a two to four-fold elevated risk of cardiovascular disease as compared to non-diabetic individuals. Hence, long-term uncontrolled hyperglycemia, which is known by measuring HbA1c levels, is strongly speculated of supporting atherogenesis. Increased glucose is converted into advanced glycation end products (AGEs) which not only make blood vessels lose its elasticity but also make them stenotic and activates chronic inflammation. In addition, AGEs have been confined to fatty streaks, atherosclerotic lesions, lipid-containing smooth muscle cells, as well as macrophages in patients with diabetes. In the study by Singh et al., patients with high CIMT had greater values of HbA1c as compared to that of normal CIMT patients and this was nearly significant statistically ($P = 0.06$). However, HbA1c levels were significantly associated with stroke patients showing carotid arteries plaque ($P = 0.008$).[25]

The mean creatinine was also found to be significantly higher in the high-CIMT sub-group ($p<0.05$), which may be because of uncontrolled nature of diabetes mellitus in these patients leading to nephropathy features. In addition, the mean cholesterol, mean triglyceride as well as mean LDL were found to be significantly higher in the high-CIMT group, which again shows that deranged lipid parameters were more commonly linked to high CIMT in T2DM. Dyslipidemia have been found to speed up the processes which ultimately lead to plaque formation in the circulation in the initial stages of diabetes mellitus, and they may further worsen atherosclerosis in the diabetic patient as were supported by the results noted in our study.[23] The various fractions of lipid profile stated a strong relationship with CIMT in the diabetic patients. This relationship was equally strong with serum total cholesterol, serum triglycerides as well as serum LDL, while serum HDL levels showed no significant relationship with high or low CIMT noted in the study. The findings of athero-embolic disease were found to be significantly associated with high-CIMT as well ($p<0.05$). Hence, it can be stated that obesity, higher serum diabetes indicators, deranged creatinine as well as deranged lipid profile parameters were found to be significantly linked with high CIMT in the study ($p<0.05$).

In the study by Butt et al., significant association was found between DM duration, BMI as well as cholesterol derangement, and these findings were replicated in our study as well.[23] In the study by Bonora et al., CIMT was raised in T2DM patients who had high central obesity, indicated by increased waist circumference, a finding replicated in our study as well.[26] Another study by Ciccone et al. also found that BMI was strongly associated with CIMT which suggests that central fat accumulation may accelerate the atherosclerotic change and possibly also explain the increased atherosclerosis incidence in patients suffering from obesity.[27] In the study by Gayathri et al., some findings identical to that in our study was the increased waist circumference in the high-CIMT group, as well as significant association between the higher CIMT and atheroembolic events. However, unlike our study, dyslipidemia was not found to have any association with high CIMT in this study by Gayathri et al.[12] In the study by Kota et al., a strong correlation was found between CIMT and lipid profile parameters, HbA1c and PPBS which were similar findings to that in our study.[21] In a study by Bashir et al., significant positive correlation was found between CIMT and lipid parameters, while other findings were not significant. This finding again was replicated in present study.[28]

Present study had a lot of strong points. The overall occurrence of high CIMT was assessed, and then relation of various patient factors was analyzed with CIMT in the T2DM patients. This is a definite valuable addition to the Indian evidence in relation to the topic. However, our study did have few limitations. The study was done only at one center, with a limited number of patients. In addition, we did not compare the findings with the non-diabetic patients, and it was a one arm study. Also, the baseline CIMT assessment was only considered in the study. Future studies with larger sample size, conducted at multiple centers and comparative studies with non-diabetic patients may also help in validating our evidence and confirming our findings.

CONCLUSION

Large number of patients with type 2 DM were found to be having high CIMT. This indicates that DM is associated with atherosclerotic risk in many cases. In addition, the patients with high CIMT were found to have significantly higher BMI and waist circumference, worse glycemic parameters, worse renal function, worse lipid parameters as well as greater evidence of atheroembolic disease which indicates the greater presence of atherosclerotic risk factors in this set of patients. This indicates that CIMT has a great predictive value and can act as an important indicator for atherosclerosis.

FUNDING

No funding sources

CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

REFERENCES

1. WHO. Diabetes Factsheet. Accessed from https://www.who.int/news-room/fact-sheets/detail/diabetes. Last accessed on 15th December 2020.
2. International Diabetes Federation. IDF Diabetes Atlas — 7th Edition. Diabetes Atlas Accessed from http://www.diabetesatlas.org/. Last accessed on 16th December 2020.
3. Tripathy J, Thakur J, Jeet G, Chawla S, Jain S, Pal A et al. Prevalence and risk factors of diabetes in a large community-based study in North India: results from a STEPS survey in Punjab, India. Diabetes Metab Synd. 2017;9(1):1-8.
4. Sibal L, Agarwal SC, Home PD. Carotid intima-media thickness as a surrogate marker of cardiovascular disease in diabetes. Diabetes MetabSyndrObes2011;4:23-34.
5. Wong M, Edelstein J, Wollman J, Bond MG. Ultrasonic-pathological comparison of the human arterial wall. Verification of intima-media thickness. ArteriosclerThromb1993;13:482-6.
6. Nambi V, Chambless L, He M, Folsom AR, Mosley T, Boerwinkle E, et al. Common carotid artery intima-media thickness is as good as carotid intima-media thickness of all carotid artery segments in improving prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. Eur Heart J 2012;33:183-90.
7. Sinha AK, Eigenbrodt M, Mehta JL. Does carotid intima media thickness indicate coronary atherosclerosis? CurrOpinCardiol2002;17:526-30.
8. Frouse Jr. An evaluation of methods for imaging and quantifying coronary and carotid lumen stenosis and Atherosclerosis. Circulation 1993;87(II):1117-33.
9. Jacoby DS, Mohler ER 3rd, Rader DJ. Noninvasive atherosclerosis imaging for predicting cardiovascular events and assessing therapeutic interventions. CurrAtheroscler Rep 2004;6:20-26.
10. Van der Meer IM, Iglesias del Sol A, Hak AE, Bots ML, Hofman A, Witteman JC, et al. Risk factors for progression of atherosclerosis measured at multiple sites in the arterial tree: The Rotterdam study. Stroke 2003;34:2374-79.

11. Agarwal AK, Gupta PK, Singla S, Garg U, Prasad A, Yadav R, et al. Carotid intimomedial thickness in type 2 diabetic patients and its correlation with coronary risk factors. J Assoc Physicians India 2008;56:581-86.
12. Gayathri R, Chandni R, Udayabhaskaran V. Carotid Artery Intima Media Thickness in Relation with Atherosclerotic Risk Factors in Patients with Type 2 Diabetes Mellitus. J Assoc Physicians India 2012;60:20-24.
13. Donahoe SM, Stewart GC, McCabe CH, Mohanavelu S, Murphy SA, Cannon CP, et al. Diabetes and mortality following acute coronary syndromes. JAMA 2007;298:765–75.
14. Sone H, Tanaka S, Iimuro S, Oida K, Yamasaki Y, Oikawa S, et al. Serum level of triglycerides is a potent risk factor comparable to LDL cholesterol for coronary heart disease in Japanese patients with type 2 diabetes: subanalysis of the Japan Diabetes Complications Study (JDCS). J Clin Endocrinol Metab2011;96:3448–56.
15. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson Jr SK. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults, Cardiovascular Health Study Collaborative Research Group. N Engl J Med 1999;340:14–22.
16. Yoshida M, Mita T, Yamamoto R, Shimizu T, Ikeda F, Ohmura C, et al. Combination of the Framingham risk score and carotid intima-media thickness improves the prediction of cardiovascular events in patients with type 2 diabetes. Diab Care 2012;35:178–80.
17. Yamasaki Y, Kodama M, Nishizawa H, Sakamoto K, Matsuhisa M, Kajimoto Y, et al. Carotid intima-media thickness in Japanese type 2 diabetic subjects: predictors of progression and relationship with incident coronary heart disease. Diab Care 2000;23:1310–15.
18. Polak JF, Pencina MJ, O'Leary DH, D'Agostino RB. Common carotid artery intima-media thickness progression as a predictor of stroke in multi-ethnic study of atherosclerosis. Stroke 2011;42:3017–21.
19. Zanchetti A, Hennig M, Hollweck R, Bond G, Tang R, Cuspidi C, et al. Baseline values but not treatment-induced changes in carotid intima-media thickness predict incident cardiovascular events in treated hypertensive patients: findings in the European Lacidipine Study on Atherosclerosis (ELSA). Circulation 2009;120:1084–90.
20. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Volzke H, Tuomainen TP, et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a metaanalysis of individual participant data. Lancet 2012;379:2053–62.
21. Kota SK, Mahapatra GB, Kota SK, Naveed S, Tripathy PR, Jammula S, et al. Carotid intima media thickness in type 2 diabetes mellitus with ischemic stroke. Indian J EndocrMetab2013;17:716-22.
22. Okayama KI, Mita T, Gosho M, Yamamoto R, Yoshida M, Kanazawa A et al. Carotid intima-media thickness progression predicts cardiovascular events in Japanese patients with type 2 diabetes. Diab Res and Clin Prac. 2013;101:286-92.
23. Butt MRA, Zakaria M. Association of Common Carotid Intimal Medial Thickness (CCA-IMT) with risk factors of atherosclerosis in patients with type 2 diabetes mellitus. J Pak Med Assoc. 2009;59(9):590-93.
24. 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.
25. Singh AS, Atam V, Chaudhary SC, et al. Relation of glycated hemoglobin with carotid atherosclerosis in ischemic stroke patients: An observational study in Indian population. Ann Indian Acad Neurol. 2013;16(2):185-89.
26. Bonora E, Tessari R, Micciolo R, Zenere M, Targher G, Padovani R, et al. Intimalmedial thickness of the carotid artery in nondiabetic and NIDDM patients. Relationship with insulin resistance. Diab Care 1997;20:627-31.
27. Ciccone M, Maiorano A, De Pergola G, Minenna A, Giorgino R, Rizzon P. Microcirculatory damage of common carotid artery wall in obese and non-obese subjects. Clin HemorheolMicrocirc1999;21:365-74.
28. Bashir F, Nageen A, Kidwai SS, Ara J. Carotid intima-media thickness and cardiometabolic risk factors in Pakistani type 2 diabetics. Saudi J Health Sci 2017;6:145-50.