How to Cite:
Damle, A. J., Thorat, S. T., Kasireddy, S. R., Yeleshwaram, V. R., & Mehta, P. J. (2022). Relation of carotid intima media thickness (CIMT) with fasting and postprandial triglyceride levels in subjects with type 2 diabetes mellitus: A comparative study. *International Journal of Health Sciences*, *6*(S1), 4100–4118. https://doi.org/10.53730/ijhs.v6nS1.5749

Relation of carotid intima media thickness (CIMT) with fasting and postprandial triglyceride levels in subjects with type 2 diabetes mellitus: A comparative study

Avanti J. Damle
Resident, Department of Medicine, Krishna Institute of Medical Sciences (Deemed to Be University), Karad (Maharashtra), India

Sanjay T. Thorat
Professor, Department of Medicine, Krishna Institute of Medical Sciences (Deemed to Be University), Karad (Maharashtra), India

Shivamsh R. Kasireddy
Resident, Department of Medicine, Krishna Institute of Medical Sciences (Deemed to Be University), Karad (Maharashtra), India

Vignesh R. Yeleshwaram
Resident, Department of Medicine, Krishna Institute of Medical Sciences (Deemed to Be University), Karad (Maharashtra), India

Pranav J. Mehta
Resident, Department of Medicine, Krishna Institute of Medical Sciences (Deemed to Be University), Karad (Maharashtra), India

***Abstract*---**Objectives: The lipid abnormalities seen in Type 2 Diabetes Mellitus (T2DM), especially hypertriglyceridemia, undoubtedly contribute to higher risk of atherosclerotic cardiovascular disease (ASCVD). Carotid intima media thickness (CIMT) measurement is a suitable non-invasive method to detect early changes of atherosclerosis. As atherosclerosis is increasingly being recognized as a postprandial event, the present study is aimed to study the correlation between fasting and postprandial triglyceride levels with CIMT in patients with T2DM. Materials and Method: 106 T2DM patients in the age group 30 to 75 years with duration of initial diagnosis of T2DM ≥ 5years, without ischemic heart disease, cerebrovascular disease and peripheral vascular disease were recruited in this single centre, cross sectional, observational study. CIMT was measured in all patients using B mode ultrasonography.

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
***Corresponding author**: Avanti J. Damle*
Manuscript submitted: 18 Jan 2022, Manuscript revised: 09 Feb 2022, Accepted for publication: 27 March 2022

Fasting and postprandial blood glucose levels, glycosylated Hb (HbA1c), renal function tests, fasting and postprandial triglyceride levels (FTG, PPTG), total cholesterol, HDL, LDL and VLDL were measured. Results: The study population was divided into 3 groups based on fasting and postprandial triglyceride levels: Group A (FTG <150 mg/dl, PPTG <200 mg/dl), Group B (FTG <150 mg/dl, PPTG ≥200 mg/dl) and Group C (FTG ≥150mg/dl, PPTG ≥ 200 mg/dl). The mean CIMT in individuals in Group C was significantly higher than those in Group A (p < 0.001). Significantly higher CIMT was also present in Group B vs Group A (p < 0.001). However, there was no such statistically significant difference among Group B and Group C pertaining to the mean CIMT. Group B and Group C were found to have higher number of individuals with CIMT > 0.9mm whereas all individuals from Group A had CIMT between 0.5mm to 0.9mm. FTG and PPTG both had a significant, moderately positive correlation with CIMT, with PPTG having a more positive correlation as compared to fasting levels (r = 0.63 vs r = 0.57). CIMT also had a weak positive, but statistically significant correlation with BMI (r = 0.322, p < 0.05), HbA1c (r = 0.344, p < 0.05) and VLDL (r = 0.261, p < 0.05). Conclusion: Isolated elevation in postprandial triglyceride levels may present as a better and early indicator of dyslipidemia related to atherosclerosis in Type 2 diabetes mellitus.

***Keywords*---**carotid intima media thickness, hypertriglyceridemia, diabetes.

Introduction

The global burden of diabetes mellitus continues to increase and is presenting to be the fastest growing health challenges of the 21st century. As per the International Diabetes Federation, 463 million adults are living with diabetes mellitus, this number having tripled in the past 20 years. It is estimated that by 2030 there will be 578 million adults with diabetes and 700 million by 2045. [1]
In India, the prevalence of diabetes in adults is 8.9%. Currently 77 million people in India are suffering from diabetes mellitus, making it the second most affected country in the world. [2] India is at the epicentre of this diabetes pandemic. Lower age at onset and lower levels of body mass index (BMI) characterizes Type 2 diabetes mellitus (T2DM) in Asian Indians as compared to the western population. [3]

Diabetes is associated with high cardiovascular morbidity and mortality. The Framingham Heart study showed a marked increase in peripheral artery disease, coronary artery disease, myocardial infarction and heart failure in patients with diabetes.[4] Asian Indian population with T2DM especially has a higher risk of developing coronary artery disease.[3] This increase in cardiovascular disease (CVD) seems to be due to the sum effect of hyperglycemia with other cardiovascular risk factors like dyslipidemia, hypertension, obesity, cigarette smoking and low physical activity. Additionally, albuminuria, reduced glomerular filtration rate (GFR), abnormal platelet function, increased markers of

inflammation and endothelial dysfunction contribute to higher prevalence of CVD in this cohort of patients.

Hyperlipidemia seems to be associated with insulin resistance in T2DM. Insulin resistance and the subsequent hyperinsulinemia are related to hypertriglyceridemia, elevated low-density lipoproteins (LDL), and reduced high density lipoproteins (HDL). These lipid abnormalities undoubtedly contribute to higher risk of atherosclerotic cardiovascular disease (ASCVD). Xiao et al coined the term atherogenic dyslipidemia to encompass these cluster of abnormalities: hypertriglyceridemia, low HDL cholesterol (HDL-C) levels, high small dense LDL (sdLDL) levels, elevated levels of remnant lipoproteins, and postprandial hyperlipidemia.[5] Persistently elevated triglycerides (TG) (non-fasting triglycerides ≥175 mg/dL) have been identified as one of the risk-enhancing factors by the 2018 AHA/ACC/multisociety cholesterol guideline. [6,7]Several studies have shown substantial residual risk of cardiovascular events in spite of statin therapy in diabetic patients due to persistently elevated triglyceride levels.

Atherosclerosis is increasingly being recognized as a postprandial event. Postprandial hypertriglyceridemia generally develops 3 to 6 hours after a meal. It is further exacerbated by the next meal and persists throughout the day. Thus, the vascular tree is exposed to this metabolic milieu for a majority of the day. Thus, measurement of postprandial triglyceride levels may prove to be more reliable than the fasting levels as a predictor of atherosclerotic disease especially in diabetic patients.

Atherosclerosis is generally asymptomatic till the plaque stenosis exceeds 70% to 80% of the luminal diameter after which it can lead to a reduction in blood flow. Atherosclerotic plaques can progress either chronically, with gradual luminal narrowing or acutely, or with plaque rupture and thrombosis. Hence it might prove beneficial to screen for atherosclerotic disease prior to the development of a cardiovascular or cerebrovascular event. Carotid intima media thickness (CIMT) measurement by B mode ultrasonography is a suitable non-invasive method to detect early changes of atherosclerosis. CIMT has been studied to be a marker of atherosclerosis and has been positively associated with coronary artery disease and stroke with lipid lowering agents shown to slow the progression of CIMT.[8] CIMT has also been shown to have positive correlation with elevated triglyceride levels, especially in the postprandial period. [9,10] With this background, the present study is aimed to study the correlation between fasting and postprandial triglyceride levels with CIMT in patients with Type 2 Diabetes Mellitus.

Methodology

This was a single centre, cross sectional, observational study based in a tertiary care centre conducted over period of 18 months (October 2019 to March 2021). A total of 106 participants were enrolled in the present study. It was conducted on subjects with Type 2 Diabetes Mellitus between age 30 to 75 years, at Krishna Hospital and Medical Research Centre, Karad.

Inclusion criteria

Individuals having Type 2 Diabetes Mellitus, between the ages 30 to 75 years, with duration from initial diagnosis of Type 2 DM ≥ to 5 years.

Exclusion criteria:

1. Type 1 Diabetes Mellitus patients
2. Duration from initial diagnosis of Type 2 Diabetes Mellitus < 5 years
3. Patients < 30 years or > 75 years
4. Patients with evidence of ischaemic heart disease, cerebrovascular and peripheral vascular disease.
5. Presence of other causes of hypertriglyceridemia- Hypothyroidism, Chronic liver disease, chronic kidney disease and/or nephrotic syndrome, Medication induced: Hormone related (Oral oestrogens, Tamoxifen, Raloxifene, Retinoids, Glucocorticoids), Immune related (Cyclosporine, Tacrolimus, Interferon)
6. Patients receiving lipid lowering drugs- Statins, Fenofibrates

Institutional Ethics Committee (IEC) [Protocol number: 217/2019-2020] approval was taken. The written and informed consent was taken from all the participants in local and English language before including them in to the study.

The enrolled subjects underwent bilateral carotid artery Doppler using B mode ultrasonography with 7.5MHz transducer on Siemens Acuson Juniper VA10 ultrasound machine, to determine the intimal medial thickness. The intima media thickness was measured at 3 sites- at the carotid bulb, 1cm proximal and 1 cm distal to the bulb. It was measured from the leading edge of the first echogenic line- representing the interface between the lumen and the intima, to that of the second echogenic line- which represented the junction between the media and the adventitia. The mean value from the three measurements was calculated. The mean value of the right and left CIMT was considered for analysis.

After an overnight fast of 12 hours, blood samples were drawn to analyse the fasting blood glucose (BSL F) levels and the fasting lipid profile (Total cholesterol, LDL, HDL and fasting Triglycerides- FTG). Patients, after taking insulin or OHAs, took a standard meal of 9kcal/kg (60–65% energy provided by carbohydrate, 15–20% by protein, and 20% by fat). Postprandial blood glucose (BSL PP) was measured 2 hours post meal. Postprandial triglyceride (PPTG) levels were assessed from samples drawn 4 hours post meal. Glycosylated Hb (HbA1c) and renal function tests were also studied in the study subjects.

Statistical analysis

After data collection, it was compiled and statistically analysed using Microsoft Excel and IBM SPSS version 23.1 (Trial version). It was expressed as means with standard deviation, number and percentage. Chi square test, ANOVA and Pearson correlation were used for analysis. Correlation findings (r value) were described as follows: r = 0.8 to 0.00 as strong correlation, 0.4 to 0.79 as moderate correlation and 0 to 0.39 as weak correlation. Statistical significance was considered at $p < 0.05$ at 95% confidence interval.

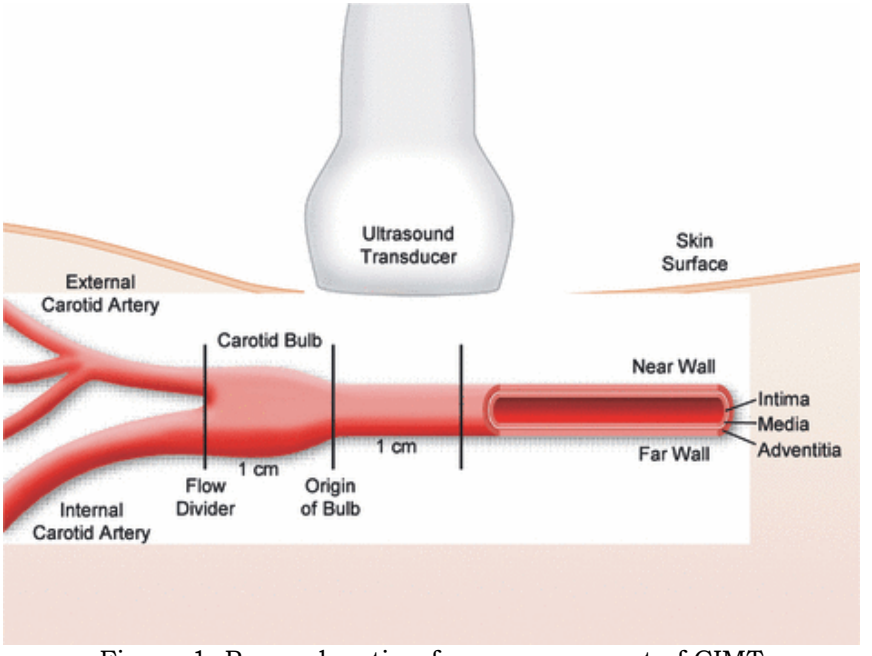
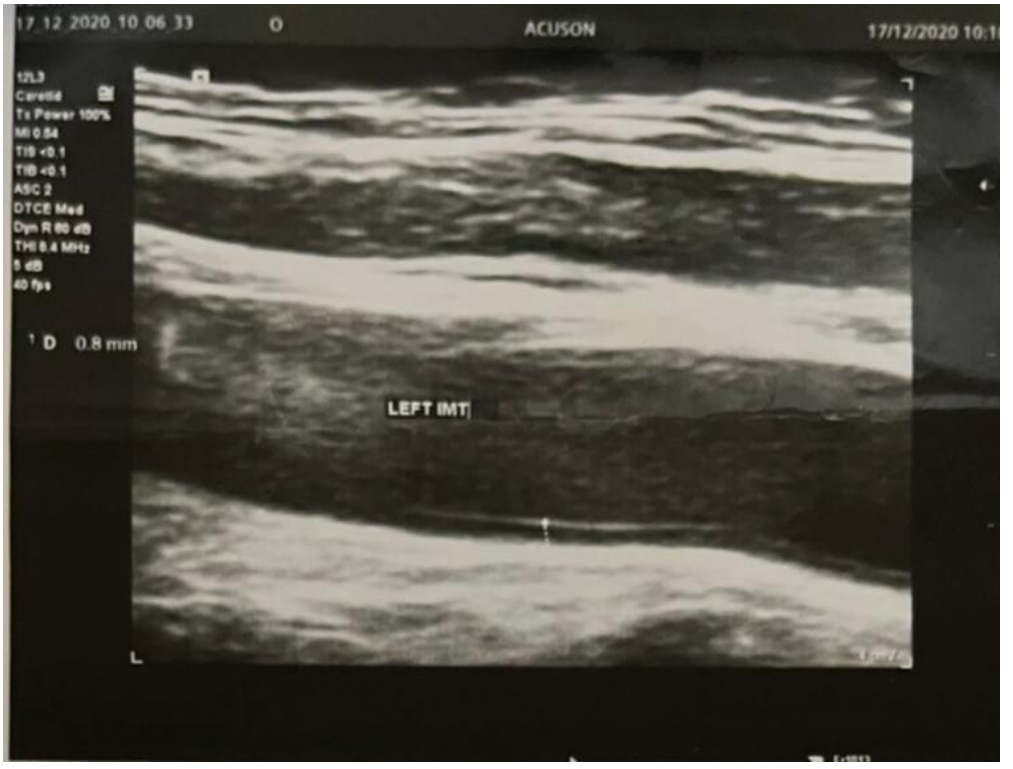


Figure 1. Proper location for measurement of CIMT



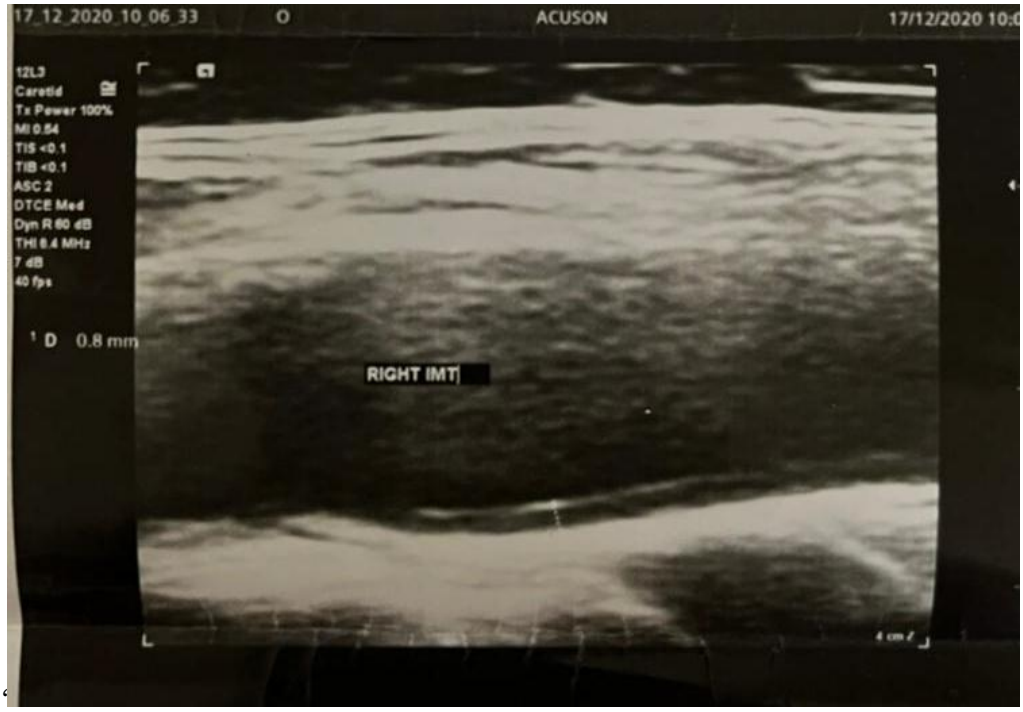


Figure 2. Carotid artery Doppler study showing intima media thickness measurement

Results

This was a cross-sectional, observational study done on 106 patients with Type 2 diabetes mellitus. The mean age of the participants was 59.58 (± 11.50) years, with a range of 32 to 75 years. The majority had age between 61 to 70 years (34.9%), followed by 51 to 60 years (24.5%). The study population had 66% males (n=70) and 34% females (n=36). The male to female ratio was 1.94:1 (X^2 = 10.91, df = 1, p < 0.001).

Baseline characteristics of all subjects

Out of the 106 subjects, 92 (86.7%) were taking oral hypoglycemic agents (OHAs) for management of diabetes while remaining 14 (13.2%) were taking insulin therapy. 57 (53.77%) individuals also had hypertension and were on treatment for the same. The mean systolic blood pressure (SBP) of the participants was 144 (± 17.13) mmHg, while the mean diastolic blood pressure (DBP) was 86.75 (± 10.50) mmHg. The range of SBP was 110 to 190 mmHg while that of DBP was 70 to 110 mmHg. The study subjects had a mean body mass index (BMI) of 25.15 (± 3.10) kg/m^2, thus predominantly falling in the overweight category. Maximum BMI was 35.20 kg/m^2, while minimum BMI was 17.31 kg/m^2. The renal function tests were in normal range, with a mean blood urea of 36.52 (± 20.82) mg/dl and the mean serum creatinine of 1.09 (± 0.34) mg/dl. The mean fasting blood glucose (BSL F) was 176.31 (± 56.71) mg/dl, and the mean postprandial blood glucose (BSL PP) was 250.26 (± 77.21) mg/dl. The mean glycosylated haemoglobin

(HbA1c) was 7.9 (± 1.78) g%, indicating fair glycaemic control. We studied the lipid profile of the participants and found the mean total cholesterol to be 159.34 (± 50.15) mg/dl, the mean low-density lipoprotein (LDL) level to be 91.94 (± 41.12) mg/dl, the mean high-density lipoprotein (HDL) level to be 40.13 (± 35.21) mg/dl and, the mean very low-density lipoprotein (VLDL) level to be 41.16 (± 28.04) mg/dl. Triglyceride levels were studied in the fasting and postprandial period. The mean fasting triglyceride (F TG) level in the participants was 164.88 (± 99.45) mg/dl, while the mean postprandial triglyceride (PP TG) level was 212.81 (± 97.14) mg/dl. Carotid Doppler study revealed the mean carotid intima media thickness (CIMT) to be 1.05 (± 0.43) mm. The maximum CIMT recorded was 1.95mm while the minimum value was 0.50 mm.

Table 1 (A)
Baseline characteristics of all subjects

Parameter	Mean ± 1SD
Age	59.58 ± 11.50 years
Duration of diabetes mellitus	9.29 ± 3.16 years
SBP	144 ± 17.13 mmHg
DBP	86.75 ± 10.50 mmHg
BMI	25.15 ± 3.10 kg/m^2
Serum urea	36.52 ± 20.82 mg/dl
Serum creatinine	1.09 ± 0.34 mg/dl
BSL F	176.31 ± 56.71mg/dl
BSL PP	250.26 ± 77.21mg/dl
HbA1c	7.9 ± 1.78g%
Total Cholesterol	159.34 ± 50.15mg/dl
LDL	91.94 ± 41.12 mg/dl
HDL	40.13 ± 35.21 mg/dl
VLDL	41.16 ± 28.04 mg/dl
F TG	164.88 ± 99.45 mg/dl
PP TG	212.81 ± 97.14 mg/dl
CIMT	1.05± 0.43 mm

Table 1 (B)
Baseline characteristics of all subjects

Parameter		Percentage
Gender	Male	70 (66%)
	Female	36 (34%)
Treatment for diabetes	Insulin	14 (13.2%)
mellitus	OHA	92 (86.7 %)
Hypertension	Present	57 (53.77%)
	Absent	49(46.22%)

Study groups:
We divided the study population into 3 groups based on fasting and postprandial triglyceride levels.

1. Group A (Normal fasting triglycerides and normal postprandial triglycerides) [NN]: FTG <150 mg/dl, PPTG <200 mg/dl

2. Group B (Normal fasting triglycerides and elevated postprandial triglycerides) [NH]: FTG <150 mg/dl, PPTG ≥200 mg/dl
3. Group C (Elevated fasting triglycerides and elevated postprandial triglycerides) [HH]: FTG ≥150mg/dl, PPTG ≥ 200 mg/dl

The Group A group had 43 individuals (40.57%), whereas Group B and Group C had 12 (11.32%) and 51 (48.11%) individuals respectively.

Table 2
Study Groups

Group	n	Percentage
Group A (NN) – FTG <150 mg/dl, PPTG<200 mg/dl	43	40.57%
Group B (NH)– FTG <150 mg/dl, PPTG >200 mg/dl	12	11.32%
Group C (HH)– FTG >150 mg/dl, PPTG > 200 mg/dl	51	48.11%

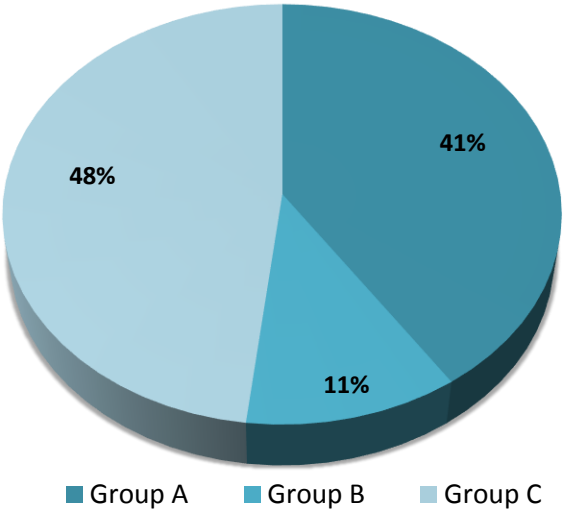


Figure 3. Study Groups

The mean age in Group A was 60.95 (± 10.08) years, while in Group B it was 57.92 (± 10.19) years. The mean age of Group C was 58.69 (± 12.18) years. There was no significant difference in the age distribution in the three groups (p = 0.251). In Group A, 15 (33.8%) were female and 28 (65.1%) were male. In Group B, 4 (33.3%) were female and 8 (66.6%) were male while in Group C, 17 (33.3%) were female and 34 (66.6%) were male. There was no significant difference in the gender distribution in the three groups. (p = 0.98)

The mean duration of diabetes in Group A, B and C was 8.20 (± 3.45) years, 8.67 (± 2.20) years and 9.35 (± 2.97) years respectively. Group B and C participants had a longer duration of diabetes than Group A. This difference was statistically significant. (p < 0.05).
The mean BSL F was 168.25 (± 48.20) mg/dl, 171.66 (± 43.25) mg/dl and 184.19 (± 66.31) mg/dl in Group A, Group B and Group C respectively. There was a significant difference in the BSL F in the three groups (p < 0.05). There was also a

significant difference in the postprandial blood glucose (BSL PP) levels in the three study groups ($p < 0.05$) with the mean BSL PP being 240.35 (± 87.12) mg/dl, 270.75 (± 59) mg/dl and 285.25 (± 82.56) mg/dl in Group A, Group B and Group C respectively. The mean HbA1c was 7.73 (± 1.89) gm% in Group A, 8.17 (± 2.48) gm % in Group B and 8.95 (± 2.92) gm% in Group C. There was a significant difference ($p < 0.05$) present with respect to glycosylated Hb in the three groups. Thus, hypertriglyceridemia was associated with poor glycaemic control.

There was a significant difference in the mean and SD of FTG and PPTG among the three groups ($p < 0.001$). No statistically significant difference was found in the distribution of the other lipid parameters in Group A, Group B and Group C. We did not find a significant difference among the three groups with respect to the anti- diabetic treatment taken, presence of hypertension, SBP, DBP, BMI and renal function tests.

Table 3
Baseline characteristics of all subjects in the study groups

Parameter	Group A (NN) (n=43)	Group B (NH) (n=12)	Group C (HH) (n=51)	p
Age	60.95 (± 10.08)	57.92 (± 10.19)	58.69 (± 12.18)	0.251
Sex (M/F)	28/15	8/4	34/17	0.98
Duration of diabetes	8.20 (± 3.45)	8.67 (± 2.20)	9.35 (± 2.97)	< 0.05*
Treatment taken for diabetes (I/OHA)	7/36	0/12	7/44	0.334
Hypertension	22 (51.16%)	4 (33.3%)	23 (45.09%)	0.535
BMI	141.16 ± 16.21	142.50 ± 16.03	147.06 ± 17.92	0.80
SBP	85.11 ± 9.09	86.33 ± 12.56	88.24 ± 11.08	0.70
DBP	24.29 ± 2.47	24.76 ± 2.43	25.97 ± 3.51	0.57
Blood urea	36.42 ± 27.21	38.25 ± 21.26	41.25 ± 28.28	0.12
Serum creatinine	0.92 ± 0.42	1.14 ± 0.23	1.16 ± 0.42	0.14
BSL F	168.25 ± 48.20	171.66 ± 43.25	184.19 ± 66.31	0.021*
BSL PP	240.35 ± 87.12	270.75 ± 59.44	285.25 ± 82.56	0.034*
Hba1c	7.73 ± 1.89	8.17 ± 2.48	8.95 ± 2.92	0.002*
Total cholesterol	144.76 ± 40.74	149.21 ± 38.52	155.35 ± 46.52	0.08
F TG	106.32 ± 25.38	128.42 ± 10.57	222.82 ±116.25	< 0.001*
PP TG	138.61 ± 35.48	221.33 ± 44.05	271.33 ± 44.05	< 0.001*
LDL	39.52 ± 11.25	37.25 ± 12.36	43.51 ± 11.36	0.24
HDL	85.16 ± 12.25	89.25 ± 14.53	92.54 ± 13.13	0.07
VLDL	30.51 ± 24.52	32.52 ± 12.53	36.25 ± 18.25	0.12

Carotid Intima Media Thickness (CIMT):
Carotid Intima Media Thickness (CIMT) was studied in all the participants. 0.63(± 0.09) mm was the mean CIMT in Group A. The mean CIMT was higher in Group B

[1.27 (± 0.39) mm] and Group C [1.33 (± 0.36) mm]. This difference was statistically significant ($p < 0.001$). In the present study, a statistically significant difference in the mean CIMT was observed in Group A vs. Group B ($p < 0.001$), as well as Group A vs. Group C ($p < 0.001$). However, there was no statistically significant difference in the mean CIMT of Group B vs. Group C ($p = 0.64$). Thus, the postprandial hypertriglyceridemia could be correlated with a higher CIMT.

Table 4
Assessment of CIMT in the study groups

	Mean CIMT (mm)	±1SD
Group A (NN) (n=43)	0.63	0.09
Group B (NH) (n=12)	1.27	0.39
Group C (HH) (n=51)	1.33	0.36

p value: Group A vs. Group B, < 0.001, Significant Difference
p value: Group A vs. Group C, < 0.001, Significant Difference
p value: Group B vs. Group C = 0.64, No significant difference

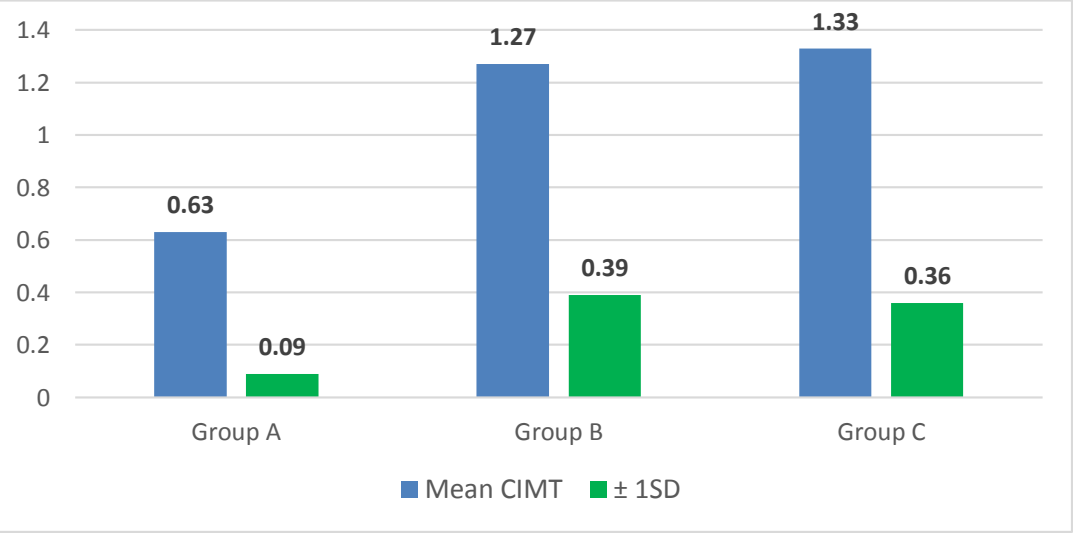


Figure 4. Assessment of CIMT in the study groups

We studied the frequency distribution of CIMT in the study groups A, B and C. All individuals in Group A had CIMT between 0.5 to 0.9 mm. Group B and Group C were found to have significantly higher number of participants with CIMT > 0.9mm. This difference between the three groups was statistically significant ($X^2 = 81.23$, df = 4, $p < 0.001$). Thus, individuals with hypertriglyceridemia had a higher CIMT.

Table 5
Distribution of CIMT in the study groups

CIMT (mm)	Group A (NN) (n=43)	Group B (NH) (n=12)	Group C (HH) (n=51)	Total
0.5 to 0.90	43 (100%)	2 (16.66%)	5 (9.8 %)	50

0.91 to 1.50	0	7 (58.33%)	33 (64.7%)	40
1.51 to 2.0	0	3 (25%)	13 (25.5%)	16

Correlation of Carotid Intima Media Thickness (CIMT) with Triglycerides

Figure 3 and 4 depict two scatter plots showing the relationship between the fasting and postprandial triglyceride levels respectively, with CIMT. The model R^2 (the coefficient of determination) for fasting triglycerides was 0.221. It was found that approximately 22% of the variation in CIMT was by the virtue of fasting triglyceride level ($p < 0.001$). The model R^2 (the coefficient of determination) for postprandial triglycerides was 0.398, thus showing that about 40% of the variation in CIMT could be accounted for by the postprandial triglyceride levels ($p < 0.001$). Fasting and postprandial triglyceride levels were both shown to have a moderately positive correlation with CIMT, with PP TG correlating more positively as compared to F TG. ($r = 0$ 63 versus $r = 0.57$)

Table 6
Correlation of CIMT and FTG

	Mean	±SD	Pearson's Correlation *r*	*p* value
CIMT (mm)	1.05	0.43	0.57	< 0.001
F TG	164.88	99.46		

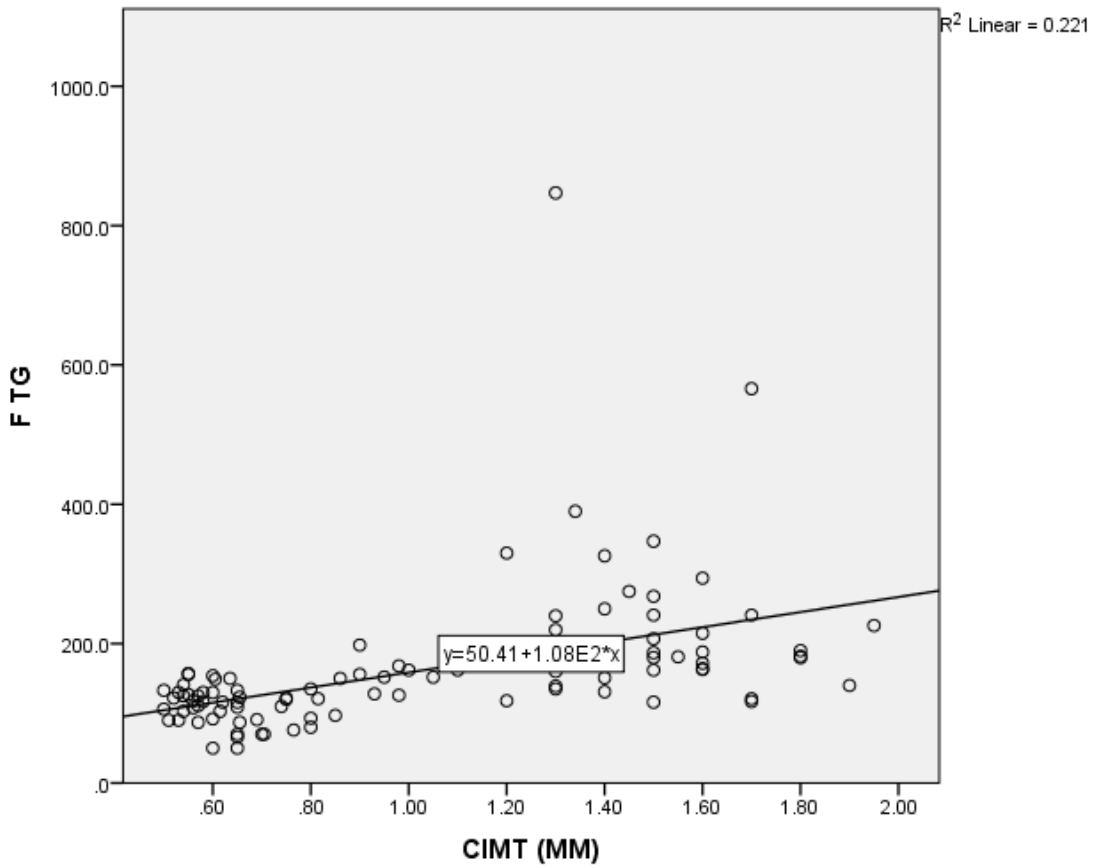


Figure 5. Correlation between FTG & CIMT

Table 7
Correlation of CIMT and PPTG

	Mean	±SD	Pearson's Correlation *r*	*p* value
CIMT (mm)	1.05	0.43	0.63	< 0.001
PPTG	212.81	97.14		

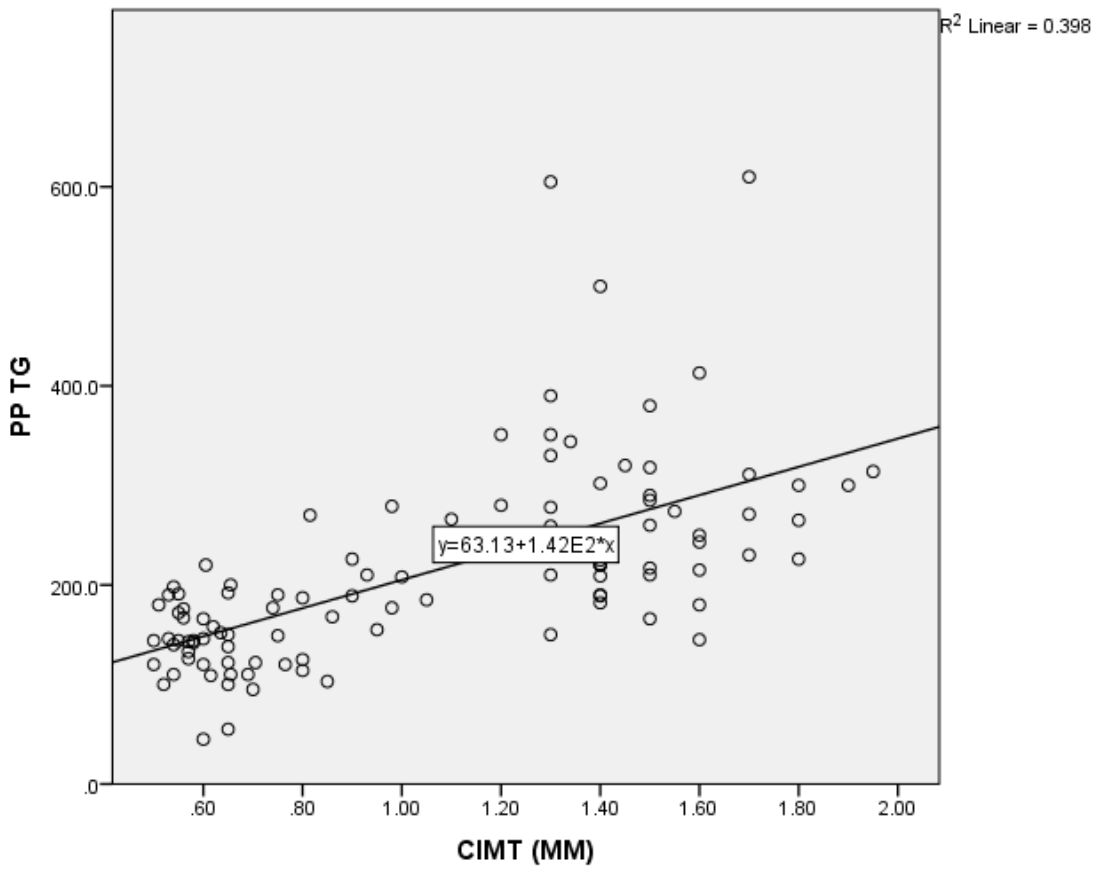


Figure 6. Correlation between PPTG & CIMT

Correlation of Carotid Intima Media Thickness (CIMT) with other parameters

On comparison of CIMT with other parameters as shown in the table below, a weak positive correlation of CIMT with BMI (r = 0.322, p < 0.05), CIMT with HbA1c (r = 0.344, p < 0.05) and CIMT with VLDL (r = 0.261, p < 0.05) was seen.

Table 8
Correlation of CIMT with other demographic and biochemical parameters

	Pearson's Correlation	*p* value
CIMT vs Age	0.071	0.469
CIMT vs Duration of diabetes	0.049	0.618
CIMT vs BMI	0.322	0.016*
CIMT vs F BSL	0.121	0.218
CIMT vs PP BSL	0.137	0.16
CIMT vs HbA1c	0.344	0.014*
CIMT vs Blood Urea	0.058	0.612

CIMT vs S Creatinine	0.021	0.83
CIMT vs Total Cholesterol	0.178	0.067
CIMT vs HDL	0.081	0.41
CIMT vs LDL	0.038	0.698
CIMT vs VLDL	0.261	0.001*
CIMT vs FTG	0.57	<0.001*
CIMT vs PPTG	0.63	<0.001*

*Significant $p < 0.05$

Discussion

106 T2DM patients who were enrolled in the study were divided into three groups- Group A (NN) i.e. subjects with normal fasting and normal postprandial triglyceride levels; Group B (NH) i.e. subjects with normal fasting and elevated postprandial triglyceride levels and Group C (HH) i.e. subjects with elevated fasting and elevated postprandial triglyceride levels. We found that the CIMT positively correlated with postprandial hypertriglyceridemia, and increase in CIMT was associated with increase in postprandial triglycerides independent of fasting triglycerides.

Sizable literature demonstrates the relationship between fasting triglyceride levels with atherosclerotic cardiovascular disease, especially in diabetic individuals. Agarwal et al found a higher intimal medial thickness in T2DM patients who had CAD, even when the CAD was not clinically overt. They found fasting triglyceride levels to be a predictor of high mean CIMT in diabetic patients with CAD, especially in patients with silent ischemia. [11] Kota SK et al also found elevated CIMT to correlate with ischemic stroke in diabetic patients. They found the cut-off point of CIMT to be 0.8mm in this population of Indian T2DM patients. A positive correlation between CIMT and fasting triglyceride levels was also established. [12] On the other hand, only few studies have evaluated the role of postprandial triglyceride levels in this regard, especially in diabetic patients.

The mean CIMT in our study population was 1.05 (± 0.43 mm). Thus, the mean CIMT being > 0.9 mm (ESC/ESH guidelines), represented an important marker for asymptomatic atherosclerosis in this cohort of diabetic patients without overt ASCVD. [13,14] The mean CIMT in Group A, Group B and Group C was 0.63 (± 0.09 mm), 1.27 (± 0.39) mm and 1.33 (± 0.36) mm respectively. This difference was statistically significant ($p < 0.001$). There was also a significant difference in the mean CIMT in the Group A as compared to Group B ($p < 0.001$). A significant difference was present in the mean CIMT of Group A vs. Group C ($p < 0.001$). However, no significant difference was seen when the mean CIMT of Group B was compared with that of Group C. We also studied the frequency distribution of CIMT in the three study groups and found a statistically significant difference ($p < 0.001$). Group B and Group C were found to have a significantly higher number of individuals with an elevated CIMT (>0.9mm). All subjects in Group A had CIMT between 0.5 to 0.9mm while only 4% of Group B subjects and 16% of Group C subjects had CIMT in this range. Both fasting and postprandial triglyceride levels were seen to have a moderately positive correlation with CIMT, with PP TG having a higher positive correlation ($r = 0.63$) as compared to F TG ($r = 0.57$). At the same time, in spite of normal fasting triglyceride levels, individuals with postprandial

hypertriglyceridemia had a higher CIMT. From this data we drew the association of postprandial hypertriglyceridemia with a higher CIMT in this study population. On comparison of CIMT with other study parameters, a statistically significant but weak positive correlation of CIMT with BMI (r = 0.322, p < 0.05), HbA1c (r = 0.344, p < 0.05) and VLDL (r = 0.261, p < 0.05) was also found.

These findings were compared with other studies present in the literature. They were similar to those of Shinichi Teno et al, who found the CIMT in the NN group to be 0.73 (± 0.13) mm, 0.86 (± 0.13) mm in the NH group (p < 0.05 vs. NN) and 0.85 (± 0.12) mm in the HH group (p < 0.01 vs. NN). No significant difference was noted in the CIMT of the NH and HH groups. There existed only a weak correlation between F TG and CIMT (p = 0.04, r = 0.27). In univariate analysis, they also found fasting total cholesterol, fasting LDL cholesterol and F TG levels as well as postprandial blood glucose, postprandial total cholesterol and PP TG levels to correlate with CIMT. However, no such association with HDL was seen. As demonstrated by multivariate analysis, postprandial plasma glucose, PP TG, and fasting LDL cholesterol levels had an independent correlation with CIMT. PP TG was found to have the most influence on CIMT (p = 0.002, standardized partial regression coefficient 0.414) amongst all these variables. [15]

Akin to the results in present study, Ahmad J et al reported the CIMT to be significantly higher in the NH [0.79 (± 0.09) mm] and HH groups [0.82 (± 0.06) mm] as compared to the NN group [0.59 (± 0.09) mm] (p < 0.001) in a study done among north Indians with T2DM. PPTG, fasting LDL, HbA1c, age as well as HOMA (homeostatic model assessment) estimated insulin resistance were found to correlate independently with CIMT. Amongst these, age and PPTG levels influenced CIMT the most (p < 0.002). [16]

In the study done by Chen X et al, CIMT in individuals with elevated postprandial triglyceride levels was significantly greater than individuals with normal postprandial triglyceride levels (0.90 mm vs 0.81 mm, p < 0.05). These findings remained significant even after adjustment for fasting triglycerides and HDL levels. [17]

Mohan V et al, reported the mean CIMT of diabetic individuals [0.95 (± 0.31) mm] to be significantly higher than that of non-diabetic individuals [0.74 (± 0.14) mm] (p < 0.001). In both diabetic and non-diabetic groups, CIMT was found to increase with age. In the diabetic population, CIMT showed positive correlation with age and duration of diabetes, however no significant correlation was seen with other parameters like total cholesterol, LDL, HDL, TG, HbA1c, BMI, waist: hip ratio, fasting insulin, insulin resistance (HOMA) or blood pressure. [18]

In contrast to above studies, Dharmalingam M et al found no significant correlation between PP TG values and CIMT, however a positive significant correlation was found between F TG and CIMT (Pearson r = 0.9043, p < 0.001, R^2 = 0.8177). [19] These findings could be explained by inclusion of only diabetic individuals with good glycaemic control (HbA1c <7%). Even in healthy individuals, literature states the presence of positive correlation between postprandial hypertriglyceridemia and CIMT, and thereby a presence of a metabolic state that points towards early atherosclerosis.

A Swedish study conducted by Boquist S et al in healthy middle-aged men found that in the fasting state, LDL cholesterol ($p < 0.05$) and basal proinsulin ($p < 0.05$) had a significant association with CIMT, however HDL and insulin did not. They also found that in the postprandial state, plasma TG at 1 to 4 hours ($p < 0.01$ at 2 hours), total triglyceride area under the curve (AUC) ($p < 0.05$), incremental triglyceride AUC ($p < 0.01$), and the large VLDL (Sf 60 to 400 apo B-100) concentration at 3 hours ($p < 0.05$) had a significant correlation with CIMT. The plasma TG 2 hours postprandial, LDL and basal proinsulin was also found to be independently related to CIMT on multivariate analysis when alcohol, tobacco consumption, waist hip circumference ratio and SBP were included as confounding factors.[10] Karpe et al also found postprandial plasma triglycerides to correlate positively with the common carotid IMT ($r = 0.44$, $p < 0.05$) in healthy middle-aged men. [20]

Table 9
Comparison of various studies

Author	Study type	Sample size (n)	Interpretation
Shinichi Teno et al[15]	Cross sectional study	n= 61	In T2 DM patients, independent of FTG, postprandial hypertriglyceridemia might be an independent risk factor for early atherosclerosis and thereby ASCVD.
Ahmad J et al[16]	Cross-sectional study	n = 86 newly diagnosed T2DM subjects	In newly diagnosed T2 DM patients (1 to 12 months duration) form North India, postprandial hypertriglyceridemia was associated with a higher CIMT, an early indicator of atherosclerosis.
Chen X et al[17]	Cross sectional study	n = 78	Elevated postprandial triglycerides may be an independent risk factor of early atherosclerosis in T2DM.
Mohan V et al[18]]	Cross sectional study	n = 243 (140 diabetics, 103 non diabetic controls)	Diabetic subjects had higher CIMT values than non-diabetic subjects. Diabetes and age were the most important risk factors associated with elevated CIMT in this South Indian cohort.
Dharmalingam M et al [19]	Cross sectional study	n =194 (145 diabetics, 49 age and sex matched controls)	Fasting hypertriglyceridemia was associated with elevated CIMT. No such correlation with postprandial triglyceride levels was found.

We also found a statistically significant difference in the BSL F, BSL PP, HbA1c and duration of diabetes in Group A, B and C. Thus increasing fasting and postprandial blood sugar levels and higher HbA1c were also associated with increasing triglyceride levels. Similarly, diabetic patients with

hypertriglyceridemia seemed to have a longer duration of diabetes mellitus. Hypertriglyceridemia was thus associated with longer duration of DM and poor glycaemic control. These findings were similar to those found in the study done by Mullugeta Y et al between HbA1c and dyslipidemia, particularly serum TG (r = 0.28, p < 0.05). They found that the group with poor glycemic control (HbA1c > 8.0 gm %) had a higher mean triglyceride level [mean TG = 190.46 (± 15.20) mg/dl] as compared to the group with good glycemic control (HbA1c ≤ 8%) [mean TG =132.05 (± 14.19) mg/dl).[21]

In contrast, Shinichi Teno et al did not report a statistically significant difference in BSL F, BSL PP and HbA1c in the NN, NH and HH groups. However this study found statistically higher total cholesterol in the HH group compared to the NN group. No such difference in LDL or HDL was found among the three study groups.[15]

Thus routine measurement of postprandial triglyceride levels may add value to risk stratification and facilitate better use of various treatment strategies for management of dyslipidemia and glycemic status in patients with T2DM. Blood sample collection is also made easier since the overnight fast for a fasting sample is not required.

The major limitation of the present study was the absence of a well matched control group and the limited sample size. The study samples only included diabetic individuals without overt ASCVD. Further research is required to assess whether the patients with postprandial hypertriglyceridemia and elevated CIMT had a higher incidence of ASCVD in the future. It would also prove beneficial to assess whether such patients with postprandial hypertriglyceridemia and higher CIMT, when started on intensive lipid lowering therapies and treatment aimed at strict glycemic control, had lower incidence of stroke, myocardial infarction, peripheral vascular disease, etc.

Conclusion

In conclusion, isolated elevation in postprandial triglyceride levels may present as a better and early indicator of dyslipidemia related to atherosclerosis. It may also benefit ease of testing by refuting the need of an 8 hour fast prior to blood sample collection. Therefore, it is important to measure postprandial triglyceride levels in diabetic individuals, as persistent postprandial hypertriglyceridemia may give rise to a pro-atherogenic environment, eventually resulting in early atherosclerosis and cardiovascular events.

Bibliography

1. Website [Internet]. Available from: International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: 2019. Available at: https://www.diabetesatlas.org
2. Members [Internet]. [cited 2021 Dec 14]. Available from: https://idf.org/our-network/regions-members/south-east-asia/members/94-india.html

3. Website [Internet]. Available from: Unnikrishnan, R., Anjana, R. & Mohan, V. Diabetes mellitus and its complications in India. Nat Rev Endocrinol 12, 357–370 (2016). https://doi.org/10.1038/nrendo.2016.53
4. The Framingham Study: An Epidemiological Investigation of Cardiovascular Disease. 1973.
5. Xiao C, Dash S, Morgantini C, Hegele RA, Lewis GF. Pharmacological Targeting of the Atherogenic Dyslipidemia Complex: The Next Frontier in CVD Prevention Beyond Lowering LDL Cholesterol. Diabetes. 2016 Jul;65(7):1767–78.
6. Virani SS, Morris PB, Agarwala A, Ballantyne CM, Birtcher KK, Kris-Etherton PM, et al. 2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients With Persistent Hypertriglyceridemia [Internet]. Vol. 78, Journal of the American College of Cardiology. 2021. p. 960–93. Available from: http://dx.doi.org/10.1016/j.jacc.2021.06.011
7. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [Internet]. Vol. 140, Circulation. 2019. Available from: http://dx.doi.org/10.1161/cir.0000000000000678
8. Chambless LE, Folsom AR, Davis V, Sharrett R, Heiss G, Sorlie P, et al. Risk factors for progression of common carotid atherosclerosis: the Atherosclerosis Risk in Communities Study, 1987-1998. Am J Epidemiol. 2002 Jan 1;155(1):38–47.
9. Ryu JE, Howard G, Craven TE, Bond MG, Hagaman AP, Crouse JR 3rd. Postprandial triglyceridemia and carotid atherosclerosis in middle-aged subjects. Stroke. 1992 Jun;23(6):823–8.
10. Boquist S, Ruotolo G, Tang R, Björkegren J, Bond MG, de Faire U, et al. Alimentary lipemia, postprandial triglyceride-rich lipoproteins, and common carotid intima-media thickness in healthy, middle-aged men. Circulation. 1999 Aug 17;100(7):723–8.
11. Agarwal AK, Gupta PK, Singla S, Garg U, Prasad A, Yadav R. Carotid intimomedial thickness in type 2 diabetic patients and its correlation with coronary risk factors. J Assoc Physicians India. 2008 Aug;56:581-6.
12. Kota SK, Mahapatra GB, Kota SK, Naveed S, Tripathy PR, Jammula S, Modi KD. Carotid intima media thickness in type 2 diabetes mellitus with ischemic stroke. Indian J Endocrinol Metab. 2013 Jul;17(4):716-22. doi: 10.4103/2230-8210.113767.
13. Simova'] ['iana. Intima-media thickness: appropriate evaluation and proper measurement [Internet]. [cited 2021 Nov 18]. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-13/Intima-media-thickness-Appropriate-evaluation-and-proper-measurement-described
14. Task Force for the management of arterial hypertension of the European Society of Hypertension; Task Force for the management of arterial hypertension of the European Society of Cardiology. 2013 ESH/ESC Guidelines for the Management of Arterial Hypertension. Blood Press. 2013 Aug;22(4):193-278. doi: 10.3109/08037051.2013.812549. Epub 2013 Jun 18. PMID: 23777479.

15. Teno S, Uto Y, Nagashima H, Endoh Y, Iwamoto Y, Omori Y, et al. Association of postprandial hypertriglyceridemia and carotid intima-media thickness in patients with type 2 diabetes [Internet]. Vol. 23, Diabetes Care. 2000. p. 1401–6. Available from: http://dx.doi.org/10.2337/diacare.23.9.1401
16. Ahmad J, Hameed B, Das G, Siddiqui MA, Ahmad I. Postprandial hypertriglyceridemia and carotid intima-media thickness in north Indian type 2 diabetic subjects. Diabetes Res Clin Pract. 2005 Aug;69(2):142–50.
17. Chen X, Tian H, Liu R. Association between fasting and postprandial triglyceride levels and carotid intima-media thickness in type 2 diabetes patients. Chin Med J . 2003 Dec;116(12):1933–5.
18. Mohan V, Ravikumar R, Shanthi Rani S, Deepa R. Intimal medial thickness of the carotid artery in South Indian diabetic and non-diabetic subjects: the Chennai Urban Population Study (CUPS). Diabetologia. 2000 Apr;43(4):494–9.
19. Dharmalingam M, Deshpande N, Vidyasagar S. Triglyceride levels and its correlation with carotid-intima-media thickness. INT. J. DIAB. DEV. COUNTRIES. 2004;24:19-22.
20. Karpe F, de Faire U, Mercuri M, Bond MG, Hellénius ML, Hamsten A. Magnitude of alimentary lipemia is related to intima-media thickness of the common carotid artery in middle-aged men. Atherosclerosis. 1998 Dec;141(2):307–14.
21. Mullugeta Y, Chawla R, Kebede T, Worku Y. Dyslipidemia associated with poor glycemic control in type 2 diabetes mellitus and the protective effect of metformin supplementation. Indian J Clin Biochem. 2012 Oct;27(4):363–9.