Relationship Between Carotid Intima Media Thickness And Lipid Profile In Type Two Diabetes Mellitus And Stage 2 Hypertension

Falgun Gosai*, Hetal Patel*,

* Assistant Professor , Department Of Medicine, GMERS Medical College, Gotri, Vadodara

Abstracts: Background & objectives: Diabetes Mellitus (DM) & hypertension (HTN) are common diseases causing premature atherosclerosis; and associated hyperlipidemia causes cardiovascular morbidity & mortality. They impose tremendous burden on healthcare system. Carotid intima-media thickness (IMT), an early marker of atherosclerosis and For every 0.1-mm increase in carotid IMT, the relative risk of ischemic heart disease increases by 15% and that of cerebrovascular disease by 18%.3 in type 2 diabetes Mellitus (DM2) patients. This study was carried out with objectives of : 1. To evaluate the prevalence of altered lipid profile in type 2 DM & stage 2 HTN & its relationship with carotid intima media thickness (CMT) as a marker of atherosclerosis.2. To study prevalence of altered lipid profile in type 2 DM & stage 2 HTN patients with respect to control subjects.3. To study additive effect of diabetes & hypertension on lipid profile & CMT . 4. Quantitative correlation of altered lipid profile & diabetic control HbA1c with CMT. 5. Relation of CMT with other established parameters like age, BMI >26kg/m^2 , total cholesterol, LDL & HDL cholesterol. **Methods:** The current prospective study has been carried out at Shree Sayaji General Hospital. From 1st September 2010 to 30th August 2011 with following group of patients who attended outdoor patient department in medicine department.1. A group of 15 type 2 Diabetes mellitus patients.2. A group of 15 stage 2 hypertensive patients.3. A group of 15 control patients. **Results:** In HTN patients, total cholesterol has positive and poor correlation while HDL cholesterol has negative & good correlation with CMT. LDL cholesterol has positive & very good correlation & VLDL cholesterol has positive &very good correlation with CMT. TC/LDL has positive & very good correlation with CMT. In DM patients, total cholesterol has positive & good relation, while HDL cholesterol has negative & good correlation with CMT.LDL cholesterol has positive & very good correlation with CMT. While VLDL cholesterol has positive & very good.TC/LDL has positive & very good correlation with CMT. While HBA1c has negative & poor correlation with CMT. The other parameters which were found to be associated with increased carotid intima media thickness were increasing age, BMI > 25 Kg/m2, post prandial blood glucose levels, high total cholesterol & low HDL cholesterol.HbA1c has not shown to be important correlation with CMT. CMT values are highly significant at p<.05 level in HTN & DM group of patients in comparison to controls. [Gosai F NJIRM 2014; 5(2) :39-45]

Key Words: carotid intima media thickness (CMT). hypertension(HTN), diabetes (DM)

Author for correspondence: Dr. Hetal Patel ,B/5 Maruti Society, Gorwa, Vadodara – 390016
E- mail: hetal.patel5210@gmail.com

Introduction: By the year 2020 cardiovascular diseases, notably atherosclerosis will become the leading global cause of total disease burden. Vascular diseases account for most morbidity and mortality in patients with diabetes mellitus and hypertension, being major risk factors for atherosclerosis.[1]

Even within a particular arterial bed, stenosis due to atherosclerosis tend to occur focally, typically in certain predisposed regions, in the extracranial circulation to the brain, the carotid bifurcation. Indeed, atherosclerotic lesions often form at branching points of arteries which are regions of disturbed blood flow .[1] Male gender, older age, smoking, hypertension, diabetes, and hypercholesterolemia are risk factors for carotid disease, as they are for stroke in general. Carotid atherosclerosis produces an estimated 10% of ischemic stroke.[1]

Diabetes causes microvascular diseases, such as nephropathy, neuropathy, and retinopathy, and macrovascular disease (e.g., atherosclerosis). Atherosclerosis of the coronary, cerebral, and peripheral arteries accounts for approximately 80 percent of mortality and for 75 percent of hospitalizations in persons with diabetes.[2]

The abnormal lipoprotein profile associated with insulin resistance, known as *diabetic dyslipidemia*, accounts for part of the elevated cardiovascular risk in patients with type 2 diabetes. [1] diabetes activates atherogenic mechanisms within vascular

smooth muscle cells, including endothelin-1,protein kinase C, RAGE, NF-kB and the production of oxidative stress. Diabetes heightens vascular smooth muscle cell migration in atherosclerotic lesions.[2]

Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease. [1 2] Carotid intima-media thickness (IMT), an early marker of atherosclerosis, is related to cardiovascular risk factors and diseases, and its measurement by means of ultrasound makes it possible to detect thickening in the initial phases of atherosclerosis.

For every 0.1-mm increase in carotid IMT, the relative risk of ischemic heart disease increases by 15% and that of cerebrovascular disease by 18%.[3] in type 2 diabetes mellitus (DM2) patients, the carotid IMT is 0.13 mm greater than in the controls. This implies an increase in age of 10 years, a circumstance that is related to a 40% higher cardiovascular risk.

Aims & Objectives:

1. To evaluate the prevalence of altered lipid profile in type 2 DM & stage 2 HTN & its relationship with carotid intima media thickness (CMT) as a marker of atherosclerosis.
2. To study prevalence of altered lipid profile in type 2 DM & stage 2 HTN patients with respect to control subjects.
3. To study additive effect of diabetes & hypertension on lipid profile & CMT .
4. Quantitative correlation of altered lipid profile & diabetic control HbA1c with CMT.
5. Relation of CMT with other established parameters like age, BMI >26kg/m^2 ,total cholesterol, LDL & HDL cholesterol.

Material and Methods: The current prospective study has been carried out at Shree Sayaji General Hospital. From 1st September 2010 to 30th August 2011 with following group of patients who attended outdoor patient department in medicine department. written and informed consent of each patients taken.

Group: 1. A group of 15 type 2 Diabetes mellitus patients.2. A group of 15 stage 2 hypertensive patients. 3. A group of 15 control patients.

Inclusion Criteria : 1. Age >30 yrs 2. Already diagnosed type 2 DM patients acc to ADA criteria 3. Already diagnosed type 2 HTN patients acc to JNC 7 criteria 4. Freshly detected DM & HTN patients.

Exclusion Criteria : 1. Age < 30 years 2. Gestational diabetes mellitus & secondary hypertension. 3. Patients on drugs that can cause DM or HTN.Like corticosteroids, thyroxine, ART drugs, estrogens, progesterone. 4. Patients of renal or hepatic diseases, chronic renal failure, nephrotic syndrome, cirrhosis.

Methods : 1. CLINICAL : All the pts were examined in detail. Patient's personal data, clinical history was elicited. Duration of disease & treatment history was noted.Detailed personal history, general examination, systemic examination was done in detail.
2. LABORATORY INVESTIGATIONS: on first meeting following investigations were done Complete blood count, Urine routine & micro examination, Blood urea & serum creatinine, ECG, Chest x-ray (PA),FBS & PP2BS,Lipid profile, Glycosylated hemoglobin, Dilated fundoscopy ,Carotid Doppler B-mode study for carotid intima-media thickness.

Result: 15 Patients of type 2 DM, 15 patients of stage 2 HTN were included with 15 controls individuals. Age & sex distribution: There are 15 males & 15 females in study group:

Table 1: Sex wise distribution of pt

	CMT IN MM	
	<=0.8	>0.8
MALE	7	8
FEMALE	5	10

Table 2: Age & Carotid Intima Media Thickness In Study Group:

AGE IN YEARS	CMT IN MM	
	≤0.8	>0.8
50-54	0	2
55-59	4	5
60-64	7	6
65-69	1	5

Out of 30 patients, female patients were having high CMT values due to higher age group among female patients.

High CMT was noted among the 50 to 54 age group (100%). it was about 55% in 55 to 59 yrs of age group. it shows there is no positive correlation between age & CIMT.The rate of change in CMT with age in cross sectional studies have shown to be .01 mm rise/yr in general population & .03 - .06mm rise/yr.

Table 3 : Relationship Between BMI (Body Mass Index) & CMT:

BMI (Body Mass Index)	CMT IN MM	
	≤0.8	>0.8
≤25	8	1 (11%)
>25	4	17(80%)

This Shows that patients with >25 BMI have 80% of having high CMT values as compared to those who are having <25 kg/m2 BMI.

Table 4: Relationship Between Smoking & CMT:

Smoking	CMT IN MM	
	≤0.8	>0.8
Non Smokers	11	10(47%)
Smokers	1	8(88%)

It clearly indicates that smoking independently associated with High CMT values up to 88%.while the non smoker individuals were having only 47% risk.

Table 5: Relationship Between Presence Of DM & CMT:

Status	CMT IN MM	
	<0.8	>0.8
Non Diabetics	11	4(23.33%)
Diabetics	7	8(53.33%)

This clearly shows that occurrence of diabetes was associated with high chances of having raised CMT values. (53% in comparison of 23%).

Table 6: Relationship Between Stage 2 HTN & CMT:

STATUS	CMT IN MM	
	<0.8	>0.8
Non Hypertensive	11	4(23.33%)
Hypertensive	5	10(75.00%)

It's evident from table that presence of hypertension is associated with up to 75% chance of having high CMT values and its complications.

Table 7: Relationship Between Stage 2 Htn & Lipid Profile (T-CHL):

Total Cholesterol	Hypertension	
	PRESENT	ABSENT
150-200	5(32%)	11
200-250	9(70.01%)	4
>250	1(100%)	0

Its clear that with high lipids almost 100% chance having hypertension….while those with less lipids shows significantly less chance of having hypertension.

Table 8: Relationship Between Type 2 & Lipid Profile (T-CHL):

Total Cholesterol	Diabetes	
	Absent	Present
150-200	11	8(42%)
200-250	4	7(63%)

Apparent from table is that higher values of cholesterol are definitely associated with presence of type 2 DM up to 63%. It shows positive correlation in the study.

Table 9: Relationship Between Hba1c & Cmt In Type 2 Dm:

HBA1c	CMT IN MM	
	<0.8	>0.8
7-7.5	5	4(44.44%)
7.6-7.9	1	5(83.33%)

This table shows positive correlation between the glycemic status & CMT. Higher HBA1c levels are associated with higher CMT values. Only 44.44% of patients having HBA1c values of 7-7.5 are having high CMT values. While 83.33% of patients were having higher CMY values if having HBA1c values between 7.6-7.9.

Table 10 : Relationship Between Cmt & Lipid Profile (T-CHL) IN STAGE 2 HTN:

Cholesterol Total	CMT IN MM	
	<0.8	>0.8
<200	4	1(20%)
200-250	1	8(88.8%)
>250	0	1(100%)

This table shows that high total cholesterol is significantly associated with high CMT values, values >250 is associated with 100% chance of having high CMT, with values of <200 it is just 20% in stage 2 hypertensive patients.

Table 11 :Relationship Between Cmt & Lipid Profile (T-CHL) IN TYPE 2 DM:

Cholesterol Total (Mg/dl)	CMT IN MM	
	<0.8	>0.8
<200	4	1(20%)
200-250	1	8(88.88%)
>250	0	1(100%)

The table is showing 100% association between highly abnormal total cholesterol is associated with high CMT values.It is directly observed proportional value. While, values between 200-250mg% has correlation of 88%. Those who were having <200mg%, shows only 20% relation with high CMT.

Table 12 : Relationship Between CMT & Lipid Profile (LDL-C) IN TYPE 2 DM:

CHOLESTEROL LDL	CMT IN MM	
	<0.8	>0.8
<100	1	0
101-129	2	3(60%)
130-159	0	7(100%)

This table is showing high LDL Cholesterol was associated with high CMT value in about 90% of cases in type 2 DM patients.

Those who are having LDL cholesterol in 101-129 shows atleast 60% and those patients with LDL of >130 shows 100% association with increased CMT.

Table 13 : Relationship Between CMT & Lipid Profile (LDL-C) IN STAGE 2 HTN:

Cholesterol LDL	CMT IN MM	
	<0.8	>0.8
<100	0	0
101-129	3	2(75%)
130-159	1	9(90%)

This table is showing high LDL Cholesterol was associated with high CMT value in about 90% of cases in stage 2 hypertensive patients.

Table 14 : Relationship Between Body Mass Index & CMT IN STAGE 2 HTN

BMI(KG/M2)	CMT IN MM	
	<0.8	>0.8
21-23.9	1	0
24-26.9	4	4(50%)
27-29.9	0	5(100%)

This table is suggestive of relation between high BMI is having higher rate of atherosclerosis. Maximum incidence is with BMI >27 are about 100%.

While those having <27 kg/M2 showed lesser CMT values. In type 2 DM patients.

Table 15 : Relationship Between Body Mass Index & CMT IN TYPE 2 DM:

BMI(KG/M2)	CMT	
	<0.8	>0.8
21-23.9	1	2(66.66%)
24-26.9	2	1(33.33%)
27-29.9	2	7(77.77%)

This table is suggestive of relation between high BMI is having higher rate of atherosclerosis. At least 77.77%. Maximum incidence is with BMI >27. While those having <27 kg/M2 showed lesser CMT values as in seen with table of 33-66% , In type 2 DM patients.

Table 16 : Relationship Between Waist Hip Ratio & CMT IN STAGE 2 HTN:

WAIST HIP RATIO	CMT IN MM	
	<0.8	>0.8
<0.9	10	2(20%)
>=0.9	1	2(66.66%)

This is the table showing that high waist hip has increased high CMT values, at least 66.66% risk in stage 2 hypertension.While those with <0.9 values are having only 20% chance of having high intima media thickness.

Table 17 : Relationship Between Waist Hip Ratio & CMT IN TYPE 2 DM:

WAIST HIP RATIO	CMT IN MM	
	<0.8	>0.8
<0.9	5	1(16.66%)
>=0.9	2	7(77.77%)

This is the table showing that high waist hip has increased chance of high CMT values at least 77.77%.While in those patients with less hip ratio shows only 16.66% chance of having high CMT value.

Table 18 : PEARSON'S COEFFICIENT

VARIABLES		N	Mean	Std. Deviation
T-CHL	1	15	194.20	17.40
	2	15	207.73	26.03
	3	15	198.07	17.91
	Total	44	200.04	21.21
HDL	1	15	44.13	6.84
	2	15	35.46	4.83
	3	15	36.85	5.08
	Total	44	38.86	6.76
LDL	1	15	122.26	18.53
	2	15	139.98	2.90
	3	15	127.07	19.06
	Total	44	129.83	21.23
VLDL	1	15	27.80	5.74
	2	15	32.28	7.74
	3	15	31.5000	7.35
	Total	44	30.5045	7.11

The analysis shows that

1. The mean of total cholesterol in control, hypertensive in diabetic group are 194.20, 207.73, and 198.07.
2. The mean of HDL cholesterol in control, hypertensive in diabetic group are 44.13, 35.46, and 36.86.
3. The mean of LDL cholesterol in control, hypertensive in diabetic group are 122.26, 139.98, and 127.07.
4. The mean of VLDL cholesterol in control, hypertensive in diabetic group are 27.8, 32.28, and 31.50.

Table 19: ANOVA test among Study Group

		F	Sig.
T-CHL	Between Groups	1.664	.202
	Within Groups		
	Total		
HDL	Between Groups	10.039	.000
	Within Groups		
	Total		
LDL	Between Groups	3.050	.058
	Within Groups		
	Total		
VLDL	Between Groups	1.746	.187
	Within Groups		
	Total		

Table 20 : SIGNIFICANCE OF CORELATION OF LIPID PROFILE & CMT IN STAGE 2 HYPERTENSIVE PATIENTS:

Sr.No.	Variable	R Value Pearson'coefficient
1	TOTAL CHOLESTEROL	.37
2	HDL	.30(Neg)
3	LDL	.72
4	VLDL	.73
5	TC/HDL	.62

Table 21: SIGNIFICANCE OF CORELATION OF LIPID PROFILE, HBA1c & CMT IN type 2 DM PATIENTS:

Sr.No.	Variable	R Value Pearson'coefficient
1	Total Cholesterol	.62
2	HDL	.72(Neg)
3	LDL	.65
4	VLDL	.65
5	TC/HDL	.63
6	Hb1AC	.44

Normal value of pearson's coefficient is -1 to 1. If R value is between .5 to 1..it suggests good correlation. If between 0 to .5 and poor correlation. Positive and negative correlation can be explained.

Discussion: Macro vascular complications in case of DM & HTN are the leading cause of morbidity & mortality all over the world.As these patients are having multiple risk factors for atherosclerosis, the risk of having ischemic heart disease & cerebrovascular diseases are 2 to 4 fold & 2 to 3 fold higher than normal population. A similar study was conducted by Shinachi et al in 2000, in Japan.4 But in that study, the correlation of postprandial lipid profile was studied in type 2 DM patients with respect to control subjects. Our is of its first kind of study that has shown an association between lipid profile & CMT in stage 2 HTN & type 2 DM patients with respect to control individuals. This study was conducted with an aim to find out the correlation

between high lipid values with carotid intima media thickness (a non invasive early marker of atherosclerosis) in type 2 DM & stage 2 HTN patients with respect to control individuals.

Comparison Of Study & Control Groups In Our Study:

1. Mean age of study in DM group is 62.4yrs. Mean age of study in HTN group is 61.2 yrs. Mean age of study in CONTROL is group 59 yrs.
2. BMI of DM group is 26.58, BMI of HTN group is 26.31,BMI of HTN group 22.39
3.Lipid study in three groups.
1. The mean of cholesterol in control, hypertensive & diabetic group are 194.20, 207.73, and 198.07 respectively.
2. The mean of HDL cholesterol in control, hypertensive & diabetic group are 44.13, 35.46, and 36.86.
3. The mean of LDL cholesterol in control, hypertensive & diabetic group are 122.26, 139.98, and 127.07.
4. The mean of VLDL cholesterol in control, hypertensive & diabetic group are 27.8, 32.28, and 31.50.

IN STAGE 2 HTN PATIENTS:

1. Total cholesterol has positive & poor **(p=0.19)** correlation with CMT.
2. HDL cholesterol has negative & good **(p=0.29 neg)** correlation with CMT.
3. LDL cholesteroL has positive & very good **(p=0.003)** correlation with CMT.
4. VLDL cholesterol has positive &very good **(p=0.003)** co relation with CMT.
5. TC/LDL has positive & very good **(p=0.01)** correlation with CMT.

IN TYPE 2 DM:

1. Total cholesterol has positive & good **(p=0.01)** correlation with CMT.
2. HDL cholesteroL has negative & good **(p=0.009neg)** correlation with CMT.
3. LDL cholesterol has positive & very good **(p=0.009)** correlation with CMT.
4. VLDL cholesterol has positive & very good **(p=0.009)** V correlation with CMT.
5. TC/LDL has positive & very good **(p=0.008)** correlation with CMT.
6. HBA1c has negative & poor **(p=0.44 neg)** correlation with CMT.

CMT values are highly significant at p<.05 level in HTN & DM group of patients in comparison to controls.However the difference between DM & HTN patients is not significant. (P>05).CMT has linear correlation with total cholesterol; LDL; VLDL; TC/LDL and no relation with HBA1c in stage 2 HTN patients in this study. This study again strengthens the earlier studies that CMT is good and effective tool to measure the preclinical atherosclerosis in stage 2 HTN and type 2 DM patients.all patients should be investigated with CMT and treated intensively with conventional measures and with drugs;with regular follow up and subsequent intervention if needed.strict sugar and BP control still remains the key factor in preventing atherosclerosis.

Initial evaluation of HTN & DM patients should include lipid profile & CMT by conventional 2D Dopler Echo, so that at risk individuals can be mobilised for either surgical carotid endarterectomy or intensive medical therapy so that serious mortality or morbidity can be prevented.

Conclusion: Carotid intima media thickness which is a marker of atheroscerosis & important cause of morbidity and mortality.

In HTN patients, total cholesterol has positive & poor correlation while HDL cholesterol has negative & good correlation with CMT. LDL cholesterol has positive & very good correlation & VLDL cholesterol has positive &very good correlation with CMT. TC/LDL has positive & very good correlation with CMT.

In DM patients, total cholesterol has positive & good relation, while HDL cholesterol has negative & good correlation with CMT.LDL cholesterol has positive & very good correlation with CMT. While VLDL cholesterol has positive & very good.TC/LDL has positive & very good correlation with CMT. While HBA1c has negative & poor correlation with CMT.

The other parameters which were found to be associated with increased carotid intima media thickness were increasing age, BMI > 25 Kg/m^2 , post prandial blood glucose levels, high total cholesterol & low HDL cholesterol. HbA1c has not shown to be important correlation with CMT. CMT values are highly significant at p<.05 level in HTN & DM group of patients in comparison to controls. However the difference between DM & HTN patients is not significant. (P>05)

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References:

1. Chan J C et al; diabetes in asia epidemiology,risk factors and pathophysiology;JAMA 301:2129,2009
2. Charmless L. E. Folsom A. R., Clegg L. X et al: Carotid wall thickness is predictive incident clinical stroke. The atherosclerosis risk in communities (ARIC) study. Am.J. Epidemiology., 151(5): 478-87, 2000
3. Anderson R. A., Envas M. L., Ellis G. R. et al: the relationship between post prandial lipemia, endothelial function and oxidative stress in healthy individuals and patients with type II diabetes. Atherosclerosis, 154(2): 474-83, 2001.
4. Shinichi Teno, Yasichiko I, Yuko et al: Association of post prandial hyper triglyceridemia and carotid intima media thicknes in patients wit5h type II diabetes. Diabetes care, 23: 1401-6,2000.
5. Mohan V., Deepak R., Ravi Kumar R.: Role of carotid intima media thickness in assessment of pre-clinical atherosclerosis. Ind. Heart. J., 52: 395-399, 2000.
6. Mohan V., Ravikumar R., Shantihirani S., Deepak R: Intimal medial thickness in the carotid artery in the south Indian Diabetic and non-diabetic subjects. Dialectologies, 43: 494-499, 2000.
7. Kieslowski J., Aragne K., Kitamine T.et al: Post-prandial hyper lipidemia in streptozotocin induced diabetic rats is due to abnormal increase in intestinal acyl Co-A: cholesterol acyl transferase. Arterioscler Thrombi. Vasc. Biol., 20(1): 171-8, 2000
8. Kasmiersk I.R., Kozubsky W., Watala C.: Intima-media complex thickness of common carotid as a risk factor for stroke. Neurogenicn 1 neurolockirugia Polaska 24(2):243-253,2000.
9. Cougfhlam B.J. Sorrentino M.J. Et Al: Does hypertriglyceridemia increase risk for CAD? G rowing evidence suggests it plays role. Post-grad. Med., 108(7):77-84, 2000.

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