



“Comparison of common carotid artery intima media thickness between diabetic patients with non-blood pressure component metabolic syndrome and diabetic patients without metabolic syndrome”

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ABSTRACT

Background and Purpose: - Patients with metabolic syndrome have greater carotid artery intima media thickness and they are at risk for generalized atherosclerosis. In this study, we planned to compare common carotid artery intima media thickness between diabetic patients with non-blood pressure component metabolic syndrome and diabetic patients without this syndrome.

Materials and Methods: - Fifty diabetic patients of both sexes with systolic blood pressure <130 mm Hg and diastolic blood pressure <85 mm Hg were subjected to high resolution B-mode ultrasonography of the common and internal carotid arteries. Patients were grouped into those without metabolic syndrome (Group I) and with non-blood pressure component metabolic syndrome (Group II).

Results:- Significantly higher mean thickness was observed in the common carotid intima media ($0.867 \pm 0.125\text{mm}$) in group II patients compared to group I patients ($0.612 \pm 0.075\text{mm}$). Group II also had significant number of patients with increased lesion intima media thickness ($\geq 1.1\text{ mm}$).

Conclusion: - Even in the absence of the blood pressure component, metabolic syndrome in type 2 diabetes mellitus patients is associated with greater common carotid intima media-thickness (IMT) values than in those who don't have metabolic syndrome.

Keywords: - Intima media thickness; Metabolic syndrome; Diabetes mellitus

INTRODUCTION:

The metabolic syndrome consists of constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus. The presence of metabolic syndrome relates to high prevalence of CVD compared to a patient with type 2 diabetes or IGT without the syndrome. ^[1] Abdominal obesity specially correlates with metabolic risk factors. Excess adipose tissue releases several products that apparently exacerbate these risk factors. They include non-esterified fatty acids (NEFA), cytokines, PAI-1, and adiponectin. High CRP levels accompanying obesity may signify cytokine excess and a proinflammatory state. An elevated PAI-1 contributes to a prothrombotic state, whereas low adiponectin levels that accompany obesity correlate with worsening of metabolic risk factors. ^[2] Insulin resistance and dysmetabolic syndrome are closely related. Insulin resistance, with its attendant hyperinsulinemia, not only contributes to the hyperglycemia of type 2 diabetes, but has also been associated, directly and indirectly, with deleterious change in the vasculature, including the progression of atherosclerosis that may ultimately lead to myocardial infarction and stroke. ^[3]

Early atherosclerosis can be detected by measuring carotid intima media thickness by using high resolution B mode ultrasonography. ^[4] B-mode ultrasonography appear to provide the most accurate in vivo assessment of early atherosclerosis, allowing visualization and measurement of intima-media thickness. In vitro and in vivo studies indicate that carotid artery IMT measurements obtained by ultrasonography correlate very well with pathologic measurements and numerous investigators have demonstrated the reproducibility of the technique. ^[5] Hypertension, duration of diabetes, hyperglycemia, and dyslipidemia are significant risk factors for stroke and associated with increased IMT. ^[6] Hassinen et al found that increase in carotid IMT was greater in elderly women who developed metabolic syndrome than those who did not in T2DM. ^[7] Many cross sectional study have shown an association of metabolic syndrome with the thickness of the carotid intima media. ^[8]

With this review we planned to compare common carotid artery intima media thickness between diabetic patients with non blood pressure component metabolic syndrome and diabetic patients without metabolic syndrome. By this, we tried to assess the

contribution of metabolic syndrome to the atherosclerotic process in type 2 diabetes.

MATERIALS AND METHODS

The study was conducted in type-2 diabetic mellitus patients attending medical OPD, diabetic clinic and admitted in various wards of Govt. medical college, Kota in year July 2009 to June 2010 after obtaining informed consent and taking permission from the Hospital Ethics Committee. The criterion of inclusion was type-2 DM. Patients were excluded if they had any previous history of ischemic stroke, hypertension, familial hyperlipidemia, history of angina, myocardial infarction, angioplasty, congestive heart failure, atrial fibrillation coronary bypass, carotid or peripheral vascular surgery, or renal insufficiency.

A total number of 50 subjects (21 females and 29 males) aged 35 to 70 years were included in study. Patients with systolic blood pressure ≤ 135 mm Hg and/or diastolic blood pressure ≤ 80 mm Hg were included in the study. Anthropometric measurements of body weight (kg), height (m), waist circumference (cm), hip circumference (cm), waist hip ratio and body mass index (BMI) were done. Biochemical analysis included fasting plasma glucose, glycosylated hemoglobin, triglycerides, low density lipoproteins, high density lipoproteins, total cholesterol, urea and creatinine.

Subjects were categorized as having non-hypertensive components of metabolic syndrome when they had at least three of the following criteria:-^[9] (1) Body mass index (BMI) ≥ 30 kg/m²; (2) Fasting plasma glucose ≥ 110 mg/dl; (3) Fasting plasma triglycerides (TG) ≥ 150 mg/dl; (4) High density lipoprotein (HDL) ≤ 40 mg/dl (men) and ≤ 50 mg/dl (women). Accordingly, the subjects were assigned to two groups, Group I, diabetic patients without metabolic syndrome and Group II, diabetic patients with non-blood pressure component metabolic syndrome.

The CCA was studied with high-resolution ultrasonography using SIEMENS G 60 system with a 7-11 MHz linear array transducer in the department of Radiodiagnosis of MBS and Associate group of Hospitals, Kota. Carotid arterial scanning was performed by a qualified, blinded radiologist in a dark, air-conditioned room. Carotid IMT is defined as the distance between the luminal border of the intima and the outer border of the media.

STATISTICAL ANALYSIS

The results are presented as absolute number, percent, median, range, and mean $\pm$ SD. The data have been analyzed by using unpaired, two-tailed Student's t-test taking $P \leq 0.05$ as the lowest limit of significance.

RESULTS

Baseline characteristics of study participants are shown in **Table 1**. Comparison of various parameters between Group I and Group II are shown in **Table 2**. Group II have significantly ($P < 0.001$) high BMI (29.08 ± 4.7 , $n=20$ vs 24.03 ± 3.19 , $n=30$), significant ($P < 0.0001$) increase in fasting serum triglycerides (164.65 ± 25.42 , $n=20$ vs 120.73 ± 28.69 , $n=30$) and significant ($P < 0.005$) decrease in high density lipoprotein (40.95 ± 4.25 , $n=20$ vs 45.27 ± 6.26 , $n=30$), significantly ($P < 0.05$) higher mean glycosylated hemoglobin (10.07 ± 1.9 , $n=20$ vs 8.44 ± 1.9 , $n=30$) than group I patients. Mean common carotid IMTs (left, right. Or both) were significantly greater in group II patients (0.867 ± 0.125 , $n=20$ vs 0.612 ± 0.075 , $n=30$) compared to group I patients. Group II had a significant number of patient with increased lesion IMT (>1.1 mm) [**Figure 1, Table 3**]. There was statistically significant positive correlation between MEAN CCA-IMT and BMI ($r = +0.5160$, $P < 0.001$) and MEAN CCA-IMT and triglyceride ($r = +0.4573$, $P < 0.001$) and statistically significant negative correlation between MEAN CCA-IMT and HDL ($r = -0.3322$, $P < 0.05$) [**Table 4**].

Table 1: Baseline characteristics of study participants

	Group I	Group II
Male	17	12
Female	13	8
Age (years)		
Male	52(35-65)	46(37-63)
Female	55(48-70)	53(38-62)
BMI (kg/m ²)		
Male	24.21 (18.18-28.65)	30.05 (21.55-32.81)
Female	22.82 (19.11-32.22)	30-24 (23.31-43.28)

Total	23.98 (18.18-30.22)	30.55 (21.55-43.28)
Fasting plasma TG(mg/dl)		
Male	126(69-190)	165 (128-198)
Female	120 (72-140)	158 (95-200)
Total	123 (69-190)	163 (95-200)
Fasting plasma HDL (mg/dl)		
Male	43 (32-54)	39 (29-49)
Female	47 (41-61)	42 (41-47)
Total	43 (32-61)	41 (29-49)
Fasting plasma Glucose (mg/dl)		
Male	152 (76-314)	179 (131-467)
Female	165 (72-321)	136 (112-215)
Total	161 (72-321)	173 (112-467)
Duration of diabetes (years)		
Male	3 (0-20)	5-5 (0-20)
Female	3 (0-12)	2 (0.25-10)
Total	3 (0-20)	4.5 (0-20)
Smokers (No.)		
Male	9	10
Female	0	0
Total	9	10

*The results are expressed as median (range); TG: Triglyceride, HDL: High density lipoprotein.

Table 2: Comparison of various parameters between Group I and Group II

PARAMETERS	GROUP 1	GROUP 2	P Value	Significance
BMI (kg/m ²)	24.03±3.19	29.02±4.7	<0.001	HS*
WHR	0.88±0.05	0.90±0.07	>0.05	NS*
FPG (mg/dl)	174.47±70.43	182.20±82.28	>0.05	NS*
HBA1c (%)	8.44±1.9	10.07±1.9	<0.05	S*
HDL (mg/dl)	45.27±6.26	40.95±4.25	<0.005	VS*
TRIGLYCERIDE (mg/dl)	120.73±28.69	164.65±25.42	<0.0001	HS*
CCA-IMT (mm)				
RIGHT	0.600±0.102	0.825±0.183	<0.0001	HS*
LEFT	0.630±0.112	0.910±0.107	<0.0001	HS*
MEAN	0.612±0.075	0.867±0.125	<0.0001	HS*
SMOKERS(n=19)	0.620±0.110	0.890±0.140	<0.0001	HS*
NONSMOKERS (n=31)	0.610±0.060	0.850±0.120	<0.0001	HS*

*HS-highly significant, VS-significant, S-significant, NS-non significant **MVA-Macro vascular accidents.

Table 3: Number of cases with increased lesion intima media thickness (IMT) [($>1.1\text{mm}$)]

	Number (percent) of Cases	
	GROUP I (n=30)	GROUP II (n=20)
RIGHT CCA-IMT	0	2(10%)*
LEFT CCA-IMT	0	2(10%)*
MEAN CCA-IMT	0	2(10%)*

*P<0.05; CCA: Common carotid artery

Table 4: Correlation between Mean common carotid artery intima media thickness (CCA-IMT) and other parameters

CORRELATION WITH CCA-IMT	'r' VALUE	P VALUE	SIGNIFICANCE
AGE (Yrs)	+0.0587	>0.05	NS
BMI (kg/m ²)	+0.5160	<0.001	HS
WHR	+0.2383	>0.05	NS
TC (mg/dl)	+0.1860	>0.05	NS
TRIGLYCERIDE (mg/dl)	+0.4573	<0.001	HS
LDL (mg/dl)	+0.2035	>0.05	NS
HDL (mg/dl)	-0.3322	<0.05	S
HBA1c (mg/dl)	+0.4772	>0.05	NS
DURATION OF DIABETES (Yrs)	+0.02351	>0.05	NS

'r' - correlation coefficient

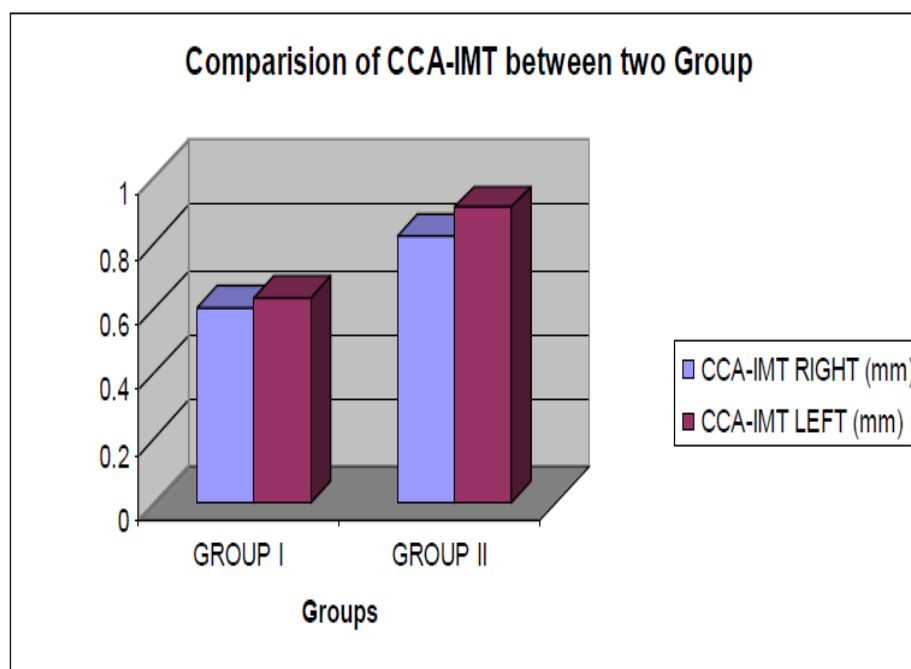


Figure 1: Comparison of common carotid artery intima media thickness (CCA-IMT) between two groups

DISCUSSION

Type 2 diabetes is an independent major risk factor for atherosclerosis.^[10] With evolution of concept of insulin resistance and description of insulin resistance syndrome, comprising of obesity, hyperlipidemia, hypertension, insulin resistance and increased risk of atherosclerosis by Reaven et al and proposal of 'common soil hypothesis' by Michael Stern et al, insulin resistance took the central stage in various studies.^[11]

Common carotid artery intima media thickness (CCA-IMT) represents a marker of subclinical atherosclerosis and helps for early detection of atherosclerosis in pre symptomatic individuals.^[12]

The objective of our study was to find whether metabolic syndrome is associated with increased common carotid artery intima media thickness in type 2 diabetic subjects. We also tried to find out correlation between common carotid artery intima media thickness and cardiovascular risk factor like age, smoking, body mass index, waist hip ratio, glycemic control and lipid profile.

In our study type 2 diabetes mellitus patients with nonblood pressure component metabolic syndrome (Group II) have significantly ($P < 0.0001$) greater mean common carotid artery IMTs (0.867 ± 0.125 , $n=20$ vs 0.612 ± 0.075 , $n=30$) than those who were free from metabolic syndrome (Group I). Similar observations were also observed by Marwan SM et al^[8] McNeil AM et al also observed that among individuals free of CHD and stroke, after adjustment for age, gender, and race, the average intimal-medial wall thickness of carotid arteries was greater among those with metabolic syndrome (747 vs 704 μm , $p < 0.0001$).^[13] This was in contrast to finding by Kovaite et al who reported that blood pressure is the most important factor for significantly high IMT values in metabolic syndrome and IMT was higher in the metabolic syndrome group.^[14]

As carotid IMT (a cut-off value of 0.75 mm reported by Holaj et al) is considered to be a marker of generalized atherosclerosis, group II patients may be considered to be at risk for future cardiovascular events as well as recurrent ischemic stroke. Carotid IMT is an independent, significant parameter for the prediction of significant coronary artery disease.^[15] Accordingly, our patients (group II) are at risk for cardiovascular events because their mean carotid IMT (left or right) is greater than 0.75 mm.

Study observations suggest that smoking has influence on CCA-IMT although the association could not achieve statistical significance. Similar was the observation of Marwan SM et al^[8] and Grethe ST et al^[16] We observed statistically significant ($p < 0.001$) strong positive correlation ($r = 0.516$) between mean CCA-IMT and BMI which is similar to Marwan SM et al^[8] and Stephanie Debette et al^[17] We

also observed positive correlation between mean CCA-IMT and WHR (waist hip ratio), though statistically not significant ($P > 0.05$) similar to Folsom AR et al^[18] In our study we found a positive correlation ($r = +0.4573$) between mean IMT and serum triglyceride and statistically significant (< 0.05) negative correlation ($r = -0.3322$) between mean IMT and serum HDL level which was similar to Marwan SM et al^[8] and Stephanie Debette et al^[17]

CONCLUSION

It is concluded from our study that even in the absence of the blood pressure component, metabolic syndrome in type 2 diabetes mellitus patients is associated with greater common carotid intima-media thickness (IMT) values than in those who don't have metabolic syndrome. CCA-IMT is also significantly associated with higher serum triglyceride level, more BMI and lower serum HDL cholesterol level. As concluded from previous studies CCA-IMT is a surrogate marker of atherosclerosis. Clinician can use increased CCA-IMT as risk stratification for vascular complications among diabetics. One should give special attention to early detection of increased CCA-IMT and treat it aggressively to decrease atherosclerosis and consequent macrovascular complications in diabetic patients.

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