Carotid Intima Media Thickness (CIMT) in Metabolic Syndrome (MS) - A Case Control Study

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ABSTRACT

BACKGROUND

Ultrasonographic B-mode measurement of the thickness of wall of major arteries is now possible. We wanted to measure the Carotid Intima Media Thickness (CIMT) and assess its correlation in subjects of Metabolic Syndrome (MS).

METHODS

This is a case control study conducted among 200 participants in Acharya Vinoba Bhave Rural Tertiary Care Hospital in central India. 100 patients with metabolic syndrome and 100 without metabolic syndrome fulfilling the inclusion and exclusion criteria were included in the study. Anthropometric measurements including height, weight, waist circumference, and BMI were recorded. Blood pressure was measured by standard methods. CIMT was measured by B-mode ultrasound as per protocol.

RESULTS

Mean age of the subjects in metabolic syndrome group and non-metabolic syndrome group was 44.93 ± 15.34 and 37.72 ± 12.83 respectively. 85% of the individuals with metabolic syndrome were obese (BMI ≥ 25 Kg/M ^{2}). Triglycerides levels were higher (>150 mg/dL) in 66% of metabolic syndrome subjects as compared to control group (10%). The mean CIMT in MS group was 0.81 ± 0.23 and in control group was (0.66 ± 0.13); the difference was statistically significant ($p<0.005$).

CONCLUSIONS

MS subjects have increased CIMT that predisposes them to future cardiovascular risk.

KEYWORDS

CIMT, Cardiovascular, BMI, Obese, Metabolic Syndrome

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BACKGROUND

Metabolic syndrome consists of constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus. Currently metabolic syndrome has increased in developing countries. In India age standardised prevalence rates of metabolic syndrome were 35.5% overall, 24.9% in males and 42.3% in females and thus it has become public health issue. MS is diagnosed with NCEP: ATPIII (National Cholesterol Education Program: adult treatment panel III) criteria.[1] MS is a risk factor for development of cardiovascular disease and type 2 diabetes mellitus. The prevalence of cardiovascular disease increases two to three times in metabolic syndrome subjects as compared to age matched controls.[2]

In recent years, the possibility of measuring a vessel using ultrasound images has gained increasing interest, in particular ultrasonographic B-mode measurement of the thickness of wall of major arteries has shown to be feasible. As in this method we try to visualise metabolic syndrome non-invasively in the arterial wall with the help of high-resolution ultrasound measurements such as measuring carotid intima-media thickness (CIMT) already proven to be surrogate end point in monitoring subclinical atherosclerosis. It has been also related with myocardial infarction, stroke and peripheral disease.[3] Metabolic syndrome increase the risk of cardiovascular morbidity and mortality.[4] It is also associated with early carotid atherosclerosis.[5] Metabolic syndrome has various parameters as discussed earlier, only few studies have enlightened on risk parameters of metabolic syndrome and CIMT.[6] Hence this study assessed the CIMT in MS subjects and compared it with healthy non obese controls.

Aim

- To estimate CIMT in metabolic syndrome subjects.

Objectives

- To compare CIMT of metabolic syndrome subjects with that of healthy non-obese controls.
- To correlate CIMT of MS subjects with anthropometric (BMI, waist circumference), clinical (blood pressure) and conventional biochemical variables (HDL, Tg, FBS) in metabolic syndrome subjects.

METHODS

Study Design

Case Control study

Study Setting

This study entitled "Carotid Intima Media Thickness (CIMT) in Metabolic Syndrome (MS) - A Case Control Study "was carried out in the Department of Medicine, Acharya Vinoba Bhave Rural Hospital (AVBRH) of Jawaharlal Nehru Medical College, DMIMS (DU), Sawangi (Meghe), Wardha; after obtaining the ethical clearance from the IEC.

Duration of Study

Six months September 2019 to February 2020).

Selection of Cases

The recruitment of the subjects for the study was done from asymptomatic university students, staff, workers, subjects attending the health camps from department of community medicine as a part of occupational health check-ups, relatives of patients admitted in the hospital. Relevant demographic data (information comprised of sex, age, race, occupation and postal address) was collected.

Informed Consent

Written informed consent was taken from the subjects and controls after explaining the nature of the evaluation to them. Each patient was subjected to a thorough history and physical examination as per the Performa.

History of Diabetes mellitus, systemic hypertension was taken, and data of any other self-reported illness was obtained. History of any chronic liver, kidney disease CAD was taken. Records of any past illness/ investigations/ treatment if available were assessed. Detailed drug history of anti-hypertensive, anti-diabetic or lipid lowering drug was obtained. Detailed physical examination and anthropometric measurement in form of height, weight, BMI, Waist circumference was calculated.

Biochemistry analysis including fasting Blood sugar (FBS), serum triglyceride (TG), high density lipoprotein (HDL), was done after fasting for 10-12 hours.

After the anthropometric data and biochemistry report analysis, the subjects were divided into 2 groups; metabolic syndrome (MS), metabolic healthy non obese (MHNO) groups.

Definition of Obesity

Obesity in this study was defined as per the body mass index (BMI) categories for Asian Indians that has been revised based on consensus guidelines. The revised guidelines define obesity as a BMI $\geq$ 25 Kg/m^2.[7]

Inclusion Criteria

Subjects after the anthropometric and biochemical analysis who had more than equal to 3 of the 5 criteria of NCEP ATP III guidelines were considered to be having MS.[8]

Metabolic syndrome (MS) is defined as per the Modified National Cholesterol Education Programme adult treatment panel III (NCEP ATP III) criteria as proposed by the AHA/NHLB. The modified NCEP criteria require at least three of the following components:

1. Abdominal obesity (waist circumference ≥90 cm for Asian men or ≥80 cm for Asian women), triglycerides ≥150 mg/dL.
2. HDL cholesterol ≤40 mg/dL for men or 50 mg/dL for women systolic/diastolic blood pressure ≥130/85 mmHg or receiving drug treatment.
3. Fasting plasma glucose ≥100 mg/dL.

For NCEP criteria abdominal obesity is a component of the syndrome but not a prerequisite for diagnosis.

Exclusion Criteria

Those MS subjects who had prior history of CAD, percutaneous coronary intervention, coronary artery bypass surgery, who had taken drugs for more than 6 months or within the previous 12 months that could potentially affect lipid metabolism. In this study, non-obese controls were defined as subjects with BMI less than 25 Kg/m^2 with less than 3 MS variables.[9]

Weight

Weight was recorded in kilograms to the nearest 0.5 kg with the subject standing motionless on the standard weighing scale without footwear and with light clothing using portable weight scale.

Height

The height was measured on the stadiometer. The subjects were instructed to stand on the stadiometer platform without any foot wears on, with the heels together and toes apart. The toes should point slightly outward approximately at 60º angle so that the back of the head, shoulder blades, buttocks, and heels make contact with the backboard. Then the standing height was measured by lowering the sadiometer headpiece so that it rests firmly on top of the participant's head, with sufficient pressure to compress the hair with the head positioned so that the top of the external auditory meatus will level with margin of bony orbit (Frankfurt's plane) and reading the measurement in centimetres.

Body Mass Index (Quetelet formula)

$$\text{BMI} = \frac{\text{Weight in Kg}}{\text{Height in Meter}^2}$$

Waist Circumference (WC in cms)

The WC in the participants was measured following the WHO STEPS protocol for measuring waist circumference (in cms). The measurement was done in male participants in a private place with only in the undergarment on. In the female participants it was ensured that at least heavy outer garments if any were removed before the measurement. The WC was measured with a non-stretchable tape at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest when person stands straight with two feet spread 25 to 30 cms apart evenly distributing the body fat during normal exhalation in a fasting state.

Blood Pressure

Blood pressures (BP) in both arms was measured with a standard mercury sphygmomanometer with a standard size cuff after one-minute rest. No smoking half hour before the measurement.[10]

Protocol

Patient seated comfortably, with back supported, legs uncrossed touching the ground, and upper arm bared. Patient's arm supported at heart level. Cuff bladder should encircle 80 percent or more of the patient's arm circumference. Mercury column should be deflated at 2 to 3 mm per second. The first and last audible sounds should be recorded as systolic and diastolic pressure, respectively. Measurements should be given to the nearest 2 mm Hg. Neither the patient nor the person taking the measurement should talk during the procedure. Mean values were determined from two independent measurements taken at 5-minute interval. In this study subjects with BP ≥ 130/85 mm of Hg or with ongoing treatment for hypertension was included as a parameter for defining MS.[11]

Biochemical Parameter Estimation

Estimation of Glucose in Plasma- Fasting plasma glucose was estimated by the GOD / POD method by the machine Robonic Semi-Automatic Chemical Analyzer.

Estimation of Serum Triglyceride- Serum triglycerides were estimated using a Liquid Stable GPO-PAP method by machine Robonic Semi-Automatic Chemical Analyzer.

Estimation of Serum HDL

Direct Enzymatic Method estimated serum HDL by machine Robonic Semi-Automatic Chemical Analyzer.

Method of Measuring Carotid Intimal Media Thickness (IMT)

Cases were examined in the supine position, the neck was oriented in 45 degree using a custom pillow, and B-mode ultrasound images were captured with 7 HZ linear array transducer in accordance with the clinical protocol recommended by the American Society of Echocardiography consensus statement, by one examiner who was unaware of participant's clinical characteristics. Common carotid artery (CCA) was scanned bilaterally (in the longitudinal and transverse views) 3 cm before carotid bifurcation, carotid bifurcation and 2 cm distal internal carotid arteries on sides

using Aloka Prosound in B-mode at AVBRH. IMT thickness was measured at plaque free segments only as the distance between the leading edge of the lumen-intima interface and media-adventitia interface. Two measurements were taken from each side and averaged; then, the mean carotid IMT was calculated as the average of measurements obtained from both CC. As per the latest ESH/ESC hypertension guidelines (2013) carotid IMT > 0.9 mm has been taken as a marker of asymptomatic organ damage.[12,13]

RESULTS

Variables		Metabolic Syndrome	Controls	P-Value
Age		44.93 ± 15.34	37.72 ± 12.83	0.0042,S
Sex		49:51	60:40	0.11,NS
Hypertension		40	15	
Diabetes Mellitus		32	8	
BMI		24 ± 4.67	21.64 ± 1.68	0.0001,S
Waist Circumference	Male	93.91 ± 9.28	77.93 ± 5.64	0.0001,S
	Female	90.41 ± 11.03	74.10 ± 4.11	0.0001,S
Systolic Blood Pressure		133 ± 15.27	121.66 ± 11.13	0.0001,S
Diastolic Blood Pressure		81.16 ± 8.43	73.80 ± 6.38	0.0001,S
Fasting Blood Sugar		97.71 ± 15.57	81.80 ± 9.91	0.0001,S
Triglyceride		175.32 ± 83.80	127.46 ± 40.86	0.0001,S
HDL	Male	37.53 ± 8.17	37.7 ± 7.14	0.33,NS
	Female	36.45 ± 7.83	42.55 ± 8.47	0.23,NS
CIMT		0.81 ± 0.23	0.66 ± 0.13	0.005,S

Table 1. Baseline Characteristics of Study and Control Groups

Model		Unstandardized Coefficients		Standardized Coefficients	t	P-Value
		B	Std. Error	Beta		
V	CIMT	-0.155	0.271			
A	Age	0.003	0.001	0.215	2.891	0.005,S
R	BMI	0.008	0.005	0.156	1.529	0.130,NS
I	WC	0.003	0.002	0.155	1.680	0.097,NS
A	FBS	0.002	0.001	0.114	1.460	0.148,NS
B	SBP	0.003	0.001	0.196	2.279	0.025,S
L	DBP	-0.005	0.002	-0.166	1.948	0.055,NS
E	HDL	-0.003	0.002	-0.118	-.612	0.110,NS
S	TG	0.001	0.000	0.221	2.944	0.004,S

Table 2. Multiple Regression Analysis of CIMT with Other Parameters

Using multiple regression analysis keeping CIMT as dependent variable; Age, SBP and TG affected CIMT in MS subjects.

Pearson's Correlation Coefficient

	Mean	Std. Deviation	N	Correlation coefficient	P-Value
CIMT	0.81	0.23	100	-	-
Age	44.93	15.34	100	0.193	0.055,NS
BMI	29.00	4.67	100	0.502	0.0001,S
WC	92.13	10.31	100	0.376	0.0001,S
FBS	97.71	15.57	100	0.327	0.0001,S
SBP	133.00	15.27	100	0.035	0.729,NS
DBP	81.16	8.43	100	0.010	0.920,NS
HDL	36.98	7.98	100	-0.065	0.518,NS
TG	175.32	83.80	100	0.429	0.0001,S

Table 3. Correlation Coefficient of CIMT with Other Parameters

Using Pearson's coefficient for analysing correlation; BMI, WC, FBS and TG had a positive linear correlation with CIMT in MS subjects.

DISCUSSION

This study estimated CIMT in cases of MS and correlated it with various anthropometric and biochemical variables of CVD risk in cases of MS. The metabolic disarrangement presents a significant risk factor for cardiovascular disease which is recognised as development of type 2 diabetes mellitus, atherosclerosis, and CVD. Metabolic syndrome is also associated with increased carotid intima media thickness, which is a surrogate preclinical marker for atherosclerosis. We found that in present study CIMT levels were high in subject of metabolic syndrome as compared to controls which was significant. These findings were in accordance with other studies in which metabolic syndrome was associated with increased CIMT progression.[14,15]

In the European Lacidipine Study on Atherosclerosis (ELSA), metabolic syndrome was associated with a 4- year change in CIMT among hypertensive subjects aged 45 to 75 years at baseline.[16] Another landmark study named; Ispessimento Medio Intimale e Rischio cardiovascular media-intima thickness and cardiovascular risk) (ISMIR) study, showed an association between metabolic syndrome and CIMT.[17]

In this study, the mean BMI in study subjects was 29 ± 4.67 which was significantly higher than the control group. Mahfouz Al-Bachie et al in their study suggested cut off for risk for metabolic syndrome which was between 23.25 to 24.35.[18] In this study the BMI was above the suggested cut off. In this study the body mass index was found strongly associated with CIMT which is in accordance with another study.[19] In this study we found no association between systolic blood pressure and CIMT these observations were in accordance with the findings of Liu CP et al,[20] which also reported no significant association between systolic blood pressure and CIMT, suggesting increased blood pressure may be a secondary development after MS.

In this study waist circumference, FBS and Tg levels strongly correlated with increased CIMT in MS subjects which was in accordance with finding of other studies.[21,22]

This observation may suggest that increased waist circumference is a risk factor that reflects long-term deviations in several metabolic risk variables. Central obesity predisposes to metabolic syndrome, hypertension, development of insulin resistance, and cardiovascular diseases. As CIMT is a surrogate marker of subclinical atherosclerosis and increase in triglyceride increase the risk of atherosclerosis and which may further increase the risk of stroke and CVD, thus there is a positive association between carotid-intima media thickness and increase in serum triglycerides.[23]

CONCLUSIONS

In metabolic syndrome the CIMT is usually abnormal. CIMT is affected by several CVD variables and also maintains a linear correlation. As CIMT is a secondary outcome,

preventive measures in form of health education, exercise, and diet are of paramount importance in subjects of metabolic syndrome.

Financial or Other Competing Interests: None.

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