ORIGINAL RESEARCH PAPER

Volume-7 | Issue-9 | September-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION OF CAROTID INTIMA MEDIA THICKNESS WITH HIGH-SENSITIVITY C-REACTIVE PROTEIN IN METABOLIC SYNDROME: A CROSS-SECTIONAL STUDY ON URBAN POPULATION IN INDIA.

Biochemistry

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ABSTRACT

Introduction: The presence of Metabolic syndrome (MetS) indicates that the individual is 2 times more vulnerable to cardiovascular disease (CVD) and 5 times to Diabetes mellitus (T2DM). Increased Carotid Intima Media Thickness (CIMT) and high-sensitivity C-reactive protein (hsCRP) are established predictors of CVD and stroke. We aimed to identify the association between CIMT and hsCRP in MetS in an urban population.

Material and Methods: This is a cross-sectional study carried out in a tertiary care hospital, Meerut. Total 200 subjects were studied including 100 cases and 100 age and sex matched healthy controls. After an overnight fast, fasting plasma glucose (FPG), lipid profile and hsCRP were performed. CIMT was measured by B-mode ultrasonography.

Results: Age and sex-adjusted CIMT among subjects with the MetS and controls was 0.78 mm ± 0.17mm, and 0.45mm ± 0.09mm ($p < 0.0001$) respectively. Biochemical parameters and hsCRP levels in MetS correlated well with CIMT more strongly than the healthy controls. The values of hsCRP were higher in subjects with MetS (4.87 ± 1.36 mg/l) and lower in healthy control (1.55 ± 0.78 mg/L) and this was statistically significant ($p < 0.0001$).

Conclusion: Recognising and focusing on the intervention of MetS as early as possible and identifying the susceptible patients who may be benefited from more aggressive preventive therapy is the key for primary prevention of diabetes and cardiovascular diseases.

KEYWORDS

Metabolic Syndrome, Cardiovascular Disease, Carotid Intima Media Thickness, High Sensitivity C-reactive Protein

INTRODUCTION

Worldwide, aging and growth of populations has led to a sharp increase in deaths because of CVD, including coronary artery disease (CAD), ischemic heart disease and stroke, in both developed and developing countries.[1] CVD has become the leading cause of almost one-third of all deaths globally.[2] Recently, the burden of CVD has become the most essential public health problem in South East Asia particularly in India and also they exhibit tendency towards central adiposity which increases their vulnerability for CVD.[3]

World Health Organization has defined stroke as the commonest life-threatening neurological disease and is the third most common cause of death surpassed only by cardiovascular disease and cancer. [3]

Inflammation has emerged as an important factor in the process of atherosclerosis, therefore hsCRP has been included as a new risk factor for CAD. [4] In a recent study it was concluded that both hsCRP and conventional lipid parameters can be used to predict the risk for CAD. The association between carotid atherosclerosis and a high risk of CVD and stroke are well established. [5]

CIMT is a non-invasive, inexpensive, rapid and reproducible measure. Increased CIMT, a proxy for carotid atherosclerosis, is a significant determinant of CVD and stroke risks. [1,2,6] Furthermore, it is well known that MetS is significantly associated with stroke, and patients with MetS are at greater risk of stroke than individuals without MetS. However, the association between hsCRP and CIMT in urban MetS population is currently unclear, especially in India.

Therefore, we aimed to explore the mean CIMT and relevant determinants of increased CIMT among individuals with different metabolic components and hsCRP in urban population in India.

MATERIAL & METHODS

Study population

This was a cross-sectional study carried out in Subharti Medical College and Chhatrapati Shivaji Subharti Hospital, Meerut in collaboration between Department of Biochemistry, Microbiology and Radio-diagnosis. Present study included patients attending the Metabolic OPD (run by Department of Biochemistry), who fulfilled the criteria of MetS proposed by International Diabetes Federation (IDF)-2005 [7] within the age group of 18 to 60 years. A total of 100 MetS patients and 100 age and sex matched healthy controls were included. Each subject's presenting complaints along with detailed past/present and family history were obtained and recorded in pre-designed proforma from individual patients.

All investigative protocols were approved by the ethical committee of Subharti Medical College, Meerut.

PHYSICAL EXAMINATION

Routine examination including height, weight, pulse, blood pressure and waist circumference were recorded. General and Systemic examination was done and findings were noted.

SAMPLE COLLECTION

After 8 to 12 hours of fasting, venous blood sample was collected under all aseptic conditions, 4 ml in plain vial for lipid profile and hsCRP, 2ml in sodium fluoride vial for FPG. The samples were transported immediately to the Central Laboratory (NABL accredited) for analysis. FPG, lipid profile was estimated using on FUSION 5.1 Chemistry System and hsCRP was estimated using ELISA kit (DRG international) on a standard ELISA reader (Readwell touch, Robonik India Pvt. Ltd.) which is well calibrated.

CIMT measurement

Bilateral carotid arteries were evaluated in the Department of Radio-diagnosis & Imaging on Samsung ACUVIX 30 ultrasound unit with high resolution linear probe of 5-10 MHz frequency on grey scale. CIMT measurements were done at the proximal, middle and distal levels of both common carotid arteries.

Statistical analysis

The data was analysed using Excel 2007, R2.8.0 Statistical Package

using SPSS for windows version 16.0 (SPSS Inc; Chicago, IL, USA). The data of the groups of MetS (case) and healthy individuals (control) were expressed as mean ± SD. Multiple logistic regression analyses was performed. Statistical significance was set at $p < 0.05$.

RESULTS

We observed that the gender distribution of the study population was; Females 46 (46.0%) & Males 54 (54.0%) among cases and 48 (48.0%) & 52 (52.0%) among controls respectively. The anthropometric measurements, biochemical parameters & hsCRP showed marked difference in subjects with MetS compared to that of subjects without MetS (p value <0.0001).

(Table 1)

TABLE 1: Anthropometric & Biochemical Parameters Of Cases And Controls.

VARIABLES	CONTROL		CASE		P- value
	MEAN	SD	MEAN	SD	
AGE	34.83	11.51	36.84	12.54	**0.3296**
WC	82.48	8.61	100.3	9.04	**<0.0001**
BMI	22.32	2.92	29.57	4.62	**<0.0001**
BP Systolic	120.43	10.48	132.6	12.45	**<0.0001**
BP Diastolic	78.01	7.88	88.66	6.41	**<0.0001**
FBS	88.48	7.61	114.42	35.68	**<0.0001**
HDL-C	48.45	8.69	37.01	7.51	**<0.0001**
TG	108.23	38.6	170.68	78.19	**<0.0001**
hsCRP	1.55	0.78	4.87	1.36	**<0.0001**
CIMT	0.45	0.09	0.78	0.17	**<0.0001**

Study population was grouped as 1 - 7, depending on presence of number of components of MetS (0, 1, 1+1, 1+2...). It was observed that the appearance of number of components of MetS was increasing, anthropometric and metabolic biochemical parameters were found to be more significantly increased except HDL which was found to be more deranged. Similar relation was observed with hsCRP and CIMT with appearance of various components of MetS. Mean hsCRP and CIMT increased from 1.02 to 6.35 mg/L and 0.39 to 0.82 mm respectively and was found to be statistically significant. (p value < 0.0001). (Table 2).

TABLE 2: Comparison between CIMT & hsCRP with increasing order of Mets components.

Groups	No. of Components	CIMT		hsCRP	
		Mean	SD	Mean	SD
1	Zero (no component)	0.39	0.09	1.02	0.61
2	1 (WC)	0.44	0.02	1.48	0.79
3	1+1 (WC + 1 components)	0.47	0.07	2.13	0.93
4	**1+2 (WC + 2 components)**	0.56	0.14	4.09	1.23
5	**1+3 (WC + 3 components)**	0.62	0.12	4.31	1.39
6	**1+4 (WC + 4 components)**	0.69	0.19	5.10	0.86
7	**1+5 (WC + 5 components)**	0.82	0.20	6.35	1.92

Further, the Pearson correlation coefficient values indicated a positive correlation between CIMT and the metabolic biochemical parameters and hsCRP. The above variables were also statistically significant. (Table 3)

TABLE 3: Correlation coefficient between CIMT with anthropometric, biochemical parameters and hsCRP.

VARIABLES	CIMT	
	r value	p value
WC	0.542	<0.0001
BMI	0.603	<0.0001
SBP	0.501	<0.0001
DBP	0.553	<0.0001
FBS	0.548	<0.0001
HDL-C	-0.362	<0.001
TG	0.628	<0.0001
HsCRP	0.574	<0.0001

DISCUSSION

The relationship between central obesity and increased levels of hsCRP has been well studied. Adipose tissue is known to secrete cytokines that stimulate the production of hsCRP in the liver. [8] We found hsCRP levels (4.87 mg/L) to be higher in centrally obese individuals with the MetS, compared to those without MetS (1.55 mg/L). Our findings correlate with several other studies which reported higher hsCRP levels in individuals with the MetS, both in obese and non-obese populations and in Caucasian and non-Caucasian populations. [9-11] Also, a linear increase in hsCRP levels with an increasing number of components of the MetS has been reported by several authors [9-11]similar to our study.

According to Ridker *et. al.*, hsCRP has been established as an independent risk factor for future cardiovascular events. It adds prognostic information to the Framingham risk score and at all levels of the metabolic syndrome. [12] The findings of our study support this opinion.

We found that presence of the MetS and the number of components were significantly associated with CIMT (Table 2). Similar findings have been reported by many authors. [13,14] We also observed an increase in CIMT between those with Zero component (Group 1) Vs those with ≥3 components (Group 4) as previously reported by Adolphe A *et. al.* [15]

CIMT is a relatively simple and non-invasive tool and an intermediate phenotype of early atherosclerosis. Increased CIMT is associated with vascular risk factors as well as the presence of more advanced atherosclerosis, which includes coronary artery disease. [15]

The small sample size was a limitation of this study. Larger epidemiological studies are needed to clarify the diagnostic value of CIMT to identify CAD, and the usefulness of hsCRP for the prediction of acute coronary syndromes in cases with increased CIMT.

CONCLUSION

The authors conclude that novel non-invasive techniques and biomarkers such as CIMT and hsCRP may help to determine the individuals who will be benefited to a large extent from these interventions. Therefore, recognizing and focusing on the intervention of metabolic state and identifying the individuals who are at high risk for developing cardiovascular events through screening and thus targeting them for individual risk evaluation and initiate appropriate management as early as possible is the key for primary prevention of MetS and CVD.

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