RELATIONSHIP OF HIGH-SENSITIVITY C- REACTIVE PROTEIN (hs-CRP) WITH THE COMPONENTS OF METABOLIC SYNDROME

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Abstract

Background: Metabolic syndrome is associated with both the development of Hypertension, Diabetes Mellitus and an increased risk of adverse cardiovascular outcome. It is considered aspro inflamatory state linked with low grade systemic inflammation. C- reactive protein is a powerful biomarker of chronic systemic inflammation. Aim of this study is to evaluate the relationship of High-sensitivity C-reactive Protein (hs-CRP)with the components of Metabolic Syndrome (MetS) among hospitalized patients.

Materials and methods: 50 patients of 18 years and above with metabolic syndrome, attending outdoor or admitted to Medicine Department of Chittagong Medical College Hospital from January 2016 to December 2016 were enrolled for this cross sectional study. The National Cholesterol Education Panel (NCEP) ATP – III, 2001 criteria was used for the diagnosis of MetS. Results: hs-CRP level was found increased in almost every components of MetSin univariate analysis but the differences were not statistically significant. Patients with MetS had higher value of hs-CRP than without MetS (5.18±1.98 Vs 3.51± 1.63mg/l) with a p value 0.023.

Conclusions: Patients with metabolic syndrome had higher levels of hs-CRP than those without metabolic syndrome and hs-CRP levels increased directly with increasing number of its components.

Key words

High sensitivity C-reactive protein; Metabolic syndrome; NCEP ATP-III.

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Introduction

Metabolic Syndrome (MetS) is defined as a constellation of abdominal obesity,triglycerides 150 mg/dL or higher, HDL cholesterol less than 40 mg/dL for men or less than 50 mg/dL for women, fasting glucose 110 mg/dL orhigher, and hypertension[1]. The prevalence of the metabolic syndrome increases with age and central adiposity is a key feature of the syndrome[2.] Around 13.4% mortality in Bangladesh is due to Cardiovascular (CV) diseases and its associatedrisk factors[3]. Prevalence of Diabetes Mellitus (DM) in Bangladesh is high among low and middle income countries (8.4 million or 10% of the population). It may increase to13% by 2030[4]. Inflammation has significant role in the development of insulin resistance and metabolic syndrome[5]. Many evidences suggest increased concentration of high sensitivity C-reactive Protein (hs-CRP) a proinflammatory cytokine is associated with insulin resistance and metabolic syndrome and may predict the onset of DM and cardiovascular events[6]. Previous studies are based on western population.High sensitivity C-reactive protein is inexpensive, standardized and widely available in Bangladesh. Studies correlatinghs-CRP and components of Metabolic Syndrome is scarce in Bangladesh. Aim of our study is to evaluate correlation of hs-CRP levels with different components of metabolic syndrome like blood pressure, waist circumference, and blood glucose.

Materials and methods

This cross sectional study conducted in the Department of Medicine of Chittagong Medical College Hospital from January 2016 to December 2016.

Inclusion criteria:

i) Patients of MetS admitted in Medicine ward and attending outdoor
ii) Age 18 years and above
iii) Having obesity as a component of metabolic syndrome.

Exclusion criteria:

i) Unwilling to give informed consent

ii) Critically ill patients (COPD with type II respiratory failure, Ischaemic heart disease with decompensated heart failure, patients requiring support of two or more organ system e.g. inotropes and haemofiltration)

iii) Patient with Familial dyslipidemia, Nephrotic syndrome, Chronic kidney disease, HBsAg or Anti HCV positive, Cirrhosis of liver, Alcoholism, chronic inflammatory disease, Hypothyroidism, Malignancy.

50 cases were enrolled who fulfilled the clinical diagnosis of obesity and gave the informed consent. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were determined on the right arm in a seated positionfor at least 5 min using a calibrated mercury sphygmomanometer. Blood pressures were determined consecutively three times and the average of the three readings was calculated. Waist circumference was measured according to report of World Health Organization Expert consultation-2008.After an overnight fast (≥8 hours) a 20-mL venous blood was collected from each participant maintaining standard laboratory techniques. Samples were collected into a Vacutainer Serum Separator Tube (SST) for analysis of lipids and glucose. After complete coagulation (30–45 minutes) the SST was centrifuged at 2500 RPM for 30 minutes. Serum was transferred from the spun SST into 3 labeled plastic tubes, first tube for glucose analysis, second for lipid panel and third tube was stored at - 20℃ to be used for hs-CRP. Glucose levels were measured by hexokinase enzymatic methods, and lipid panel was assayed by enzymatic methods and hs-CRP was analyzed by Immulite method at a standard laboratory of Chattogram. All the data were checked and edited after collection. Continuous variables were reported as the means ± SD. Means were compared using Student's t-test for two groups. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using chi-square or Fisher's exact test whichever was applicable. Correlations for hsCRP levels to components of metabolic syndrome were calculated using the correlation coefficient.Statistical significance was defined as $p < 0.05$ and confidence interval set at 95% level. SPSS (Statistical Package for Social Science) for Windows version 23 software was used for the analysis.

Results

In this study most of the patients were male (78%) and reside in urban area. Age ranges from 26 to 59 years with a median age of 56.Twenty six percent patients had history of diabetes and 58% had hypertension and all of them were taking medication regularly. Body mass index ranges from 22.31 to 34.73 kg/m^2, waist circumference ranges from 81to 100cm in female patients and 81 to 118 cm among male.

Table I : Baseline laboratory findings of the study population.

Sex of the patient		FBS (gm/dl)	Cholesterol (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	TG (mg/dl)	hs CRP (mg/dl)
Femal	Mean	6.5200	184.2727	114.1818	38.8182	152.0000	4.6727
	SD	1.41814	23.10018	18.58934	3.70994	68.89412	1.72806
Male	Mean	6.7782	209.7179	133.0333	36.4872	199.2051	4.9410
	SD	2.44940	47.12690	32.13542	5.47661	119.73923	2.10472
Total	Mean	6.7214	204.1200	128.8860	37.0000	188.8200	4.8820
	SD	2.25274	44.09805	30.55502	5.19812	111.70363	2.01430

Table II : Different components of metabolic syndrome in both sexes.

Components of MS	Male		Female		Total	
	n	%	n	%	n	p value
Central obesity *						
Present	39	100	11	100	50	--
Serum Triglyceride						
Normal	17	43.6	7	63.6	24	0.404
High (>150mg/dl)	22	56.4	4	36.4	26	
Serum HDL						
Normal	6	35.9	0	0	6	0.166
Low †	33	84.6	11	100	44	
HTN						
Absent	14	35.9	7	63.6	21	0.193
Present	25	64.1	4	36.4	29	
DM/ High FBS						
Absent	22	56.4	5	45.5	27	0.52
Present	17	43.6	6	54.5	23	

*For men waist circumference >90 cm & for women >80 cm.

† For men serum HDL <40mg/dl & for women <50 mg/dl.

❄ Taking antihypertensive or having SBP≥130mm 0f Hg / DBP ≥85 mm of Hg.

❇ FBS ≥ 110 mg/dl.

Table III : Univariate (unadjusted) association of hsCRP with components of MetS.

Components of MS	hs-CRP level		p value
	Mean	±SD	
Hypertension			
Present	5.21	2.06	0.174
Absent	4.42	1.90	
Abnormal Triglyceride			
Present	5.18	2.04	0.286
Absent	4.56	1.98	
Abnormal HDL			
Present	5.02	2.03	0.206
Absent	3.90	1.72	
Fasting plasma glucose			
Normal	4.50	2.06	0.156
High	5.32	1.92	
Metabolic syndrome			
Yes	5.18	1.68	0.023*
No	3.51	1.63	

Table IV : Odds of having elevated hs-CRP (>3mg/dl) by individual components of metabolic syndrome.

Metabolic syndrome component	OR	95% CI	p value
High triglyceride level Yes/No	2.64	.32-22.26	0.363
Low HDL level Yes/No	2.27	.211-23.85	0.49
Elevated blood pressure Yes/No	1.43	.241-8.53	0.692
Abnormal glucose metabolism Yes/No	1.29	.169-8.9	0.839
Metabolic syndrome Yes/No	1.1	.069-17.47	0.946
Sex, Male /female	0.984	.097-8.26	0.921
Age, in years	1.09	.97-1.24	0.143

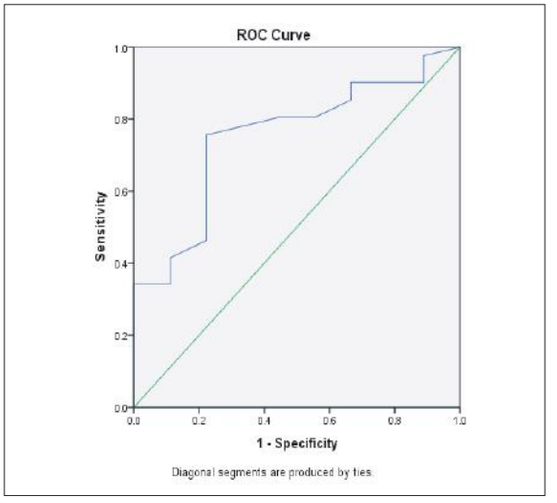

Fig 1: ROC curve to assess the utility of hsCRP to detect metabolic syndrome.

Area Under the Curve

Area	Std.Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.752	.083	.019	.590	.914

Discussion

Out of 50 patients who had central obesity, there is no difference in the prevalence of metabolic syndrome by sex (81.1% female versus 81.2% male) as in other studies[7]. In other study, the prevalence of MetS was more common in females than males[8]. Majority age group was from 45 to 60 years. Mean concentration of hs-CRP was higher inMetS (5.18±1.68 mg/l v/s 3.51±1.63 mg/l) and values increase directly with increasing number of components of the metabolic syndrome. Patients having 2, 3, and 4 risk factors had a mean hs-CRP of 4.48, 5.39 and 6.32 mg/L respectively. Bo et al also found similar findings, the mean hs-CRP for those with 0, 1, 2, 3, 4, and 5 components of the metabolic syndrome were1.9, 1.8, 2.9, 4.1, 4.1, and 5.3 mg /L.[9] Area under the ROC curve was 0.751, indicating that hs-CRP can predict the presence of the MetS in a population with central obesity. hs-CRP is a sensitive marker for acute phase inflammation and may be high with subject variability.We intended to explore the predictive value of hs-CRP measured at one time point for detecting the presence of the MetS.Several studies found higher hs-CRP levels inMetS, both in obese and non-obese populations and in Caucasian and non- Caucasian populations[10-16]. In univariate analysis most of them showed significant associations for the individual MetS components. Multivariate analysis report that central obesity was the key determinant of elevated hs-CRP levels in individuals with the MetS. Level of hs-CRP is increased marginally or not in other components of MetS[14-15]. While Aronson et al found an independent association between triglyceride level and hs-CRP. They also found associations between hs-CRP and glucose level and HDL cholesterol[17]. We found hs-CRP levels to be higher in individuals with the MetS, compared to those without.

Limitation

i) Very small sample size from a single institution and from some selected ward

ii) The present analysis was based on the single measurement of level of CRP without repeating tests

iii) Ratio of male to female is about 3.3:1. This sample was not representative of the general population.

Conclusion

In this study,patients with metabolic syndrome have significantly higher levels of hs-CRP when compared to without metabolic syndrome and hs-CRP levels increased directly with increasing number of metabolic syndrome components. Adding hs-CRP values in the diagnostic criteria for Metabolic syndrome has shown to improve future prediction of development of these diseases. Measurement of hs-CRP can be used to discriminate MetS status.

Recommendation

The association of CRP with metabolic disorder need to be further explored in the longitudinal study with larger representative sample size from different center of Bangladesh.

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Contribution of authors

MMA-Conception, acquisition of data, drafting and final approval.
MAR- Acquisition of data, drafting and final approval.
MHH- Design analysis, interpretation of data and final approval.
AB- Analysis, drafting and final approval.

Disclosure

All the authors declared no competing interest.

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