Association of hs-CRP with various components of metabolic syndrome

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ABSTRACT

Background: Metabolic syndrome is a known risk factor for atherosclerosis. Chronic inflammation plays a key role in the pathogenesis of metabolic syndrome

Objectives - The inflammatory marker C-reactive protein and its association with various components of metabolic syndrome needs further study.

Methods – In this case control study, we studied the relationship between high-sensitivity C-reactive protein (hs-CRP) with various components of metabolic syndrome in 60 subjects. 30 of them have metabolic syndrome according to adult treatment panel III (ATP III) criteria. We compared various components of metabolic syndrome like blood pressure, fasting blood sugar, waist circumference and insulin resistance with hs-CRP levels by linear regression analysis.

Results: hs-CRP levels show significant increase in metabolic syndrome group. But there is no significant correlation between hs-CRP levels and various components of metabolic syndrome like blood pressure, waist circumference and insulin resistance except for fasting blood sugar.

Conclusions: hs-CRP level in the population explains the increased cardiovascular risk in metabolic syndrome. Maintaining normal blood sugar level might help manage metabolic syndrome.

Keywords: Metabolic syndrome, hs-CRP, cardiovascular risk

INTRODUCTION

Chronic inflammation is a key component in the pathogenesis of insulin resistance and Metabolic Syndrome. In this study, we focus on the interconnection between components of metabolic syndrome like waist circumference, blood pressure, blood sugar, insulin resistance etc. and inflammation. By inhibiting insulin signal transduction, pro-inflammatory cytokines can cause insulin resistance in adipose tissue, skeletal muscle and liver. The sources of cytokines are the insulin target tissues themselves like adipose tissue, liver and the activated tissue resident macrophages. The initiating factors of this inflammatory response are not fully determined. Chronic inflammation in these tissues could cause localized insulin resistance as well as systemic insulin resistance via endocrine cytokine signaling that contribute to the abnormal metabolic state. The diagnostic category of the metabolic syndrome (MetS) is commonly used to identify cardio metabolic risk in apparently healthy individuals. [1,2] Our goal was to compare inflammatory marker level and various components of metabolic syndrome in a population of young adults and those with metabolic syndrome**.**

C-reactive protein (CRP) is the most widely studied inflammatory molecule. In healthy individuals, CRP levels are negligible. Under acute inflammatory conditions, levels of CRP in the circulation increase during the first 6 to 8 hours and reach a peak value after 48 hours[4]. CRP is a useful clinical marker because of its analytical stability, reproducible results, and commercial availability of high sensitivity assays with good precision.

Recent studies suggest that CRP may have direct pro-inflammatory effects and contributes to the initiation and progression of atherosclerotic lesions. Functionally, CRP stimulates circulating monocytes and induces their recruitment to the arterial wall. It is also involved in LDL uptake by macrophages and induces expression of cell adhesion molecules and tissue factor. Epidemiological studies during the past decade have supported the significance of CRP level in predicting future CV risk in a wide variety of clinical settings.

In the present study, we are evaluating the correlation of hs-CRP levels with different components of metabolic syndrome like blood pressure, waist circumference, blood glucose and insulin resistance. In this study, TG/HDL is used for assessing insulin resistance. Evidence show that the plasma concentration ratio of triglyceride (TG)/HDL-cholesterol may provide a simple way to identify apparently healthy insulin-resistant persons with increased cardio metabolic risk [5,6].

MATERIALS AND METHODS

This case control study was conducted in a tertiary care hospital in Kerala, India. Thirty clinically proven metabolic syndrome patients below the age of 70 years were included in the test group. Age- matched healthy control group was also selected. permission from the institutional ethics committee (M E S Medical College), the certificate number is IEC/MES/42/2014.

Informed consents obtained from all the subjects in the study. Detailed clinical, epidemiological and anthropometric characteristics were recorded.

The selection of the subjects for the study was based on the following inclusion-exclusion criteria. All the subjects included in the study were in the age group of 31 to 70 years. Metabolic syndrome was diagnosed according to the NCEP-ATP III criteria (Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults – Adult Treatment Panel III). There is no history of chronic or acute illness like cardiovascular, hepatic, renal or autoimmune diseases. The control subjects did not have any diseases, and they were not on any medication.

Height and weight were measured. Waist circumference was measured using a non-elastic measuring tape at the highest level of iliac crest with the patient standing with feet 1 foot apart[7]. BMI calculated using the equation- BMI= weight [Kg]/height[m] ^{2}. Systolic and diastolic blood pressure measured by shygmomanometer.10 ml of blood drawn from the subjects under aseptic precautions. The serum was used for estimation of Lipid profile, hs-CRP and Blood sugar. The blood samples collected were processed and analyzed at the fully automated central laboratory. Lipid profile and blood sugar estimated by a fully automated clinical chemistry analyzer (VITROS®5600 Integrated System). hs-CRP estimated by turbid metric immunoassay (Quantiamate). Results expressed as mean ± SD

Statistical Analysis

Statistical analysis was done using SPSS 20. We compared various components of metabolic syndrome like blood pressure, fasting blood sugar, and waist circumference and insulin resistance with hs-CRP levels by bivariate cross tabulation and regression analysis.

Results

The study included 60 subjects, 29 females and 31 males. The mean age of test group, (patients with metabolic syndrome) was 48.7 and that of control 53.07. The results show that there is statistically significant increase in hs-CRP levels in the test group compared to that of the control group (figure 3). Further regression analysis shows a significant predictive relation for hs-CRP for people with MS.(Table 1)

Linear regression analysis shows that none of the variables, waist circumference, systolic and diastolic BP, Fasting blood sugar or insulin resistance individually, has any significant influence on hs-CRP.(Table 2) The only significant relation was seen for

fasting blood sugar that also only in the test group.(Table 3)

Table 1:- Regression analysis showing the effect of metabolic syndrome over controls on hs-CRP

		Unstandardized Coefficients		Standardized Coefficients	t	Sig. **P value**
		B	Std. Error	Beta		
	(Constant)	.513	.289		1.778	.081
	Test or control	1.850	.408	.511	4.532	**.000**

Unit =mg/dl

Table 2:-Regression analysis of variables on hs-CRP

	Unstandardized Coefficients		Standardized Coefficients	T test	Sig.
	B	Std. Error	Beta		
(Constant)	-8.879	3.627		-2.448	**.018**
Waist circumference	.059	.071	.119	.822	**.415**
Systolic BP	.006	.014	.090	.448	**.656**
Diastolic BP	.088	.044	.323	1.974	**.054**
Fasting blood sugar	-.001	.004	-.024	-.155	**.877**
Insulin resistance	-.018	.125	-.020	-.141	**.889**

a. Dependent Variable: hs-CRP

Table 3:-Linear regression - Fasting Blood Sugar on hsCRP

Group		Sig. (P value)
Control group	(Constant)	.003
	Fasting blood sugar	.550
Test group	(Constant)	.000
	Fasting blood sugar	**.042**

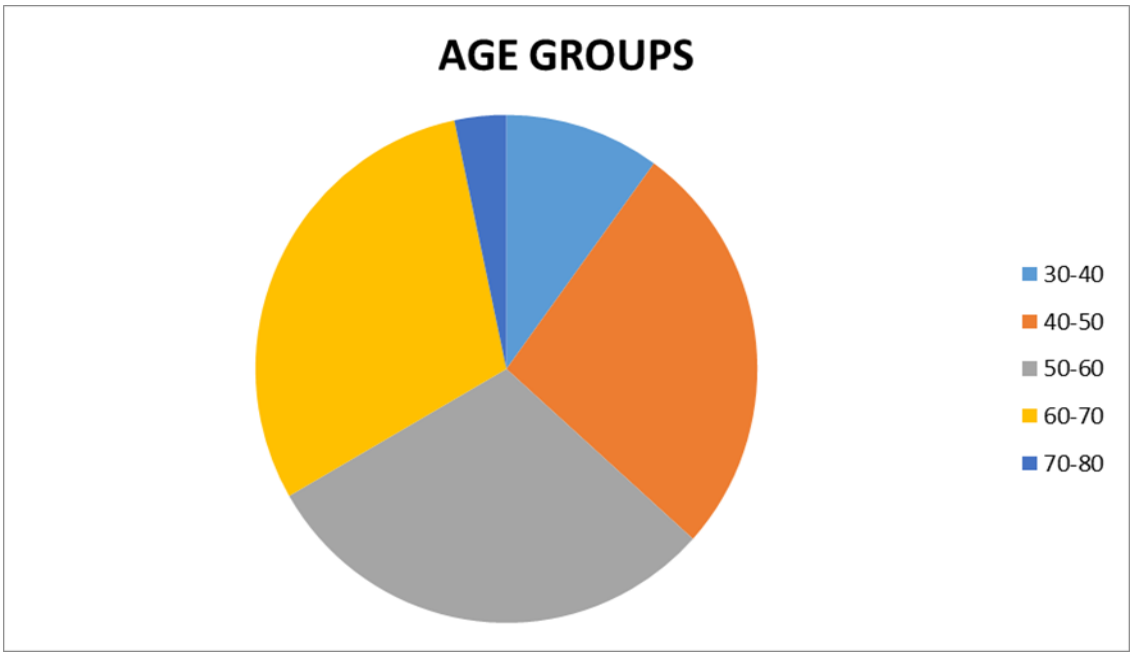

Figure 1:-Age groups in Met S. Shows higher Met S in between50-70 age groups.

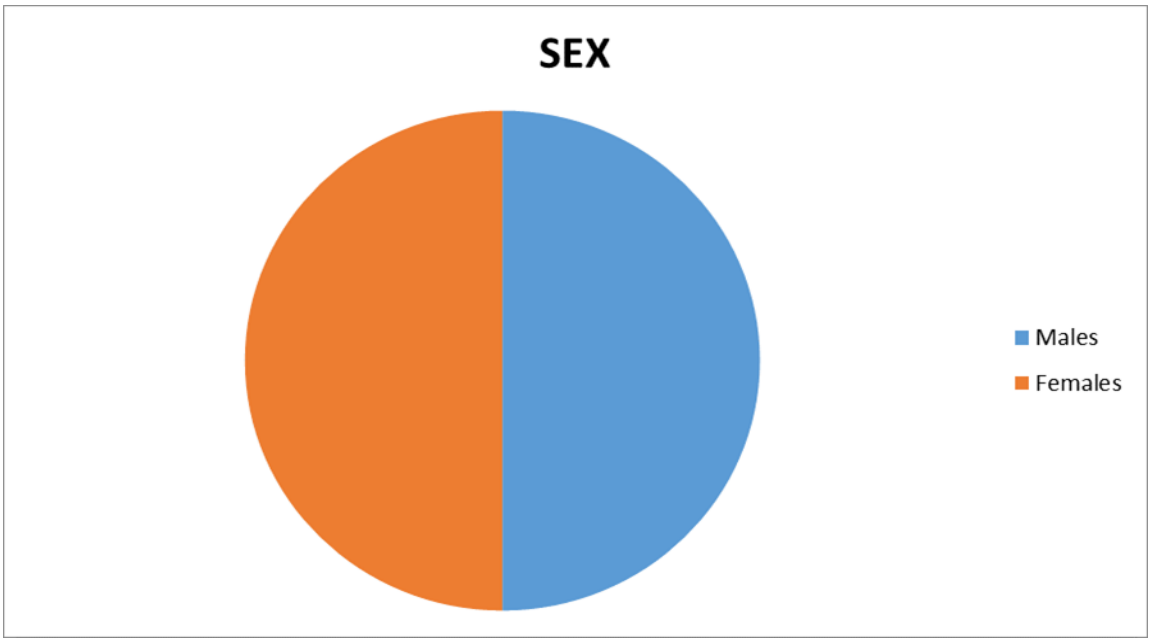

Figure 2: Representation of sex groups. Indicates equal proportion of Met S in males and females.

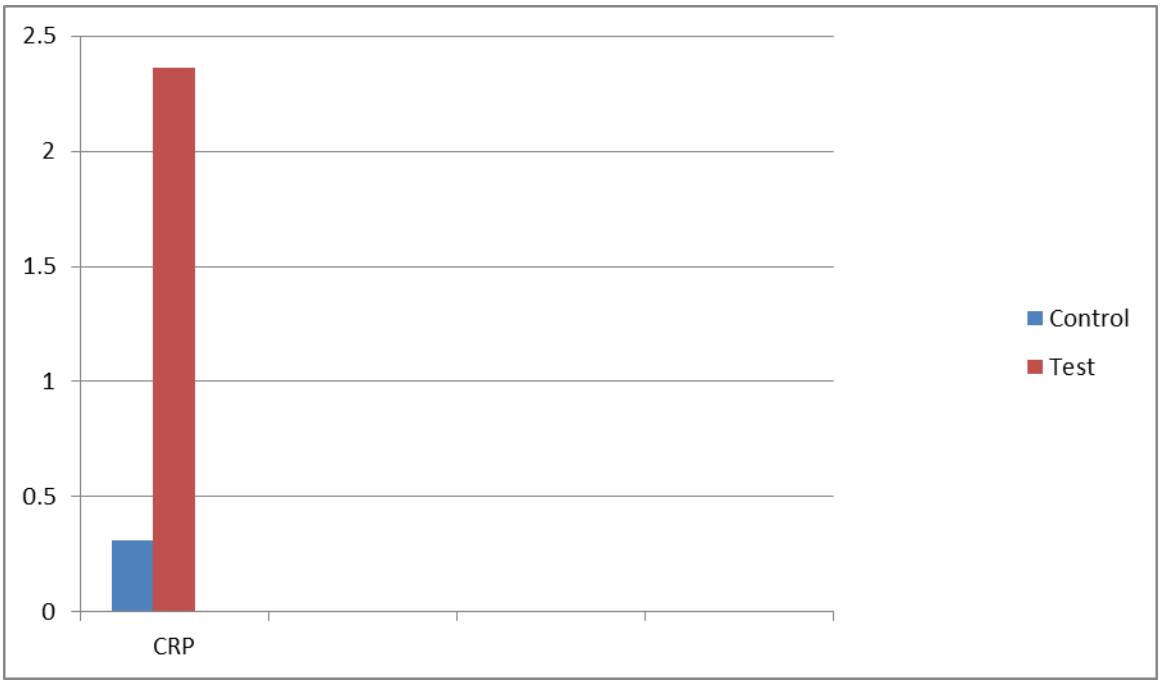

Figure 3: Graphical representation of mean± SD for hs-CRP. For control 0.31 ± 0.13 and test 2.36 ± 2.23

DISCUSSION

This study investigated hs-CRP and its association with various components of metabolic syndrome. When we analyzed our sample by sex, as in other studies [8], we found no differences in the prevalence of metabolic syndrome by sex. In some published studies, the prevalence of metabolic syndrome was more common in females than males [9]. Majority of the patients with metabolic syndrome were in the age group of 50 -70 years (60%), the next major group was patients of 40-50 years (26.6%). Only three patients (10%) were in the age group of < 40 years (figure 1). Inflammation has long been associated with metabolic syndrome and it's individual Components[10-11]. We found that participants with metabolic syndrome had significantly higher hs-CRP. Some studies show that both metabolic syndrome and elevated CRP are associated with increased incidence of cardiovascular events.

In the epidemiological studies like West of Scotland Coronary Prevention Study and Framingham Offspring Study it was shown that metabolic syndrome and hs-CRP are associated with increased cardiovascular morbidity and mortality[12-14]. When we compared the association of hs-CRP with various components of metabolic syndrome like waist circumference, systolic and diastolic BP,

Fasting blood sugar or insulin resistance individually, there was no significant association except for fasting blood sugar. A study by Gianluca Bardini et .al. shows an elevated 1-hour plasma glucose in subjects with normal glucose tolerance (NGT) and pre-diabetes is significantly associated with subclinical inflammation, high lipid ratios, and insulin resistance[15]. In our study, it is the fasting plasma glucose in patients with metabolic syndrome that shows a correlation with the inflammatory marker. Hyperglycemia acutely increases circulating cytokine concentrations by oxidative mechanisms, and this effect is more pronounced in patients with impaired glucose regulation[16]. This may be the mechanism that links elevated blood glucose to subclinical inflammation.

Among 628 healthy Japanese participants (aged 19–85 years), waist circumference was
the strongest determinant of high CRP levels[17], but our study did not show any association
between central obesity and elevated hs-CRP level.

More recently it was considered that measurement of hs-CRP should be added in the metabolic syndrome components as it was closely related to other components of the
Syndrome[18]. The treatment of several components of metabolic syndrome may have positive effects in preventing cardiovascular disease. Among the components, fasting blood sugar value has a positive correlation with hs-CRP. Preventive programs that address the importance of maintaining normal blood sugar level might help manage metabolic syndrome before cardiovascular disease develops in the population.

Small sample size (n= 60) is the main limitation of the study. These findings should be confirmed in a larger sample size and also in a prospective manner.

CONCLUSION

hs-CRP level in the test population explains the increased cardiovascular risk in metabolic syndrome. Individual components of the syndrome are not interconnected with inflammation except fasting blood sugar. Maintaining normal blood sugar level might help manage metabolic syndrome. Maintaining normal blood sugar level may prevent the progression of metabolic syndrome and development of complications.

CONFLICT OF INTEREST

We, the authors of this article declare that there are no conflicts of interest

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