# Relationship between High-sensitivity C-reactive protein and components of metabolic syndrome

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## ABSTRACT

*Metabolic syndrome is defined by a constellation of interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of cardiovascular disease, type 2 diabetes mellitus, and all-cause mortality. Recently, studies demonstrated that elevated high-sensitivity C-reactive protein concentration has emerged as an independent predictor of cardiovascular disease. The aim of this study was evaluating of association between components of metabolic syndrome and high-sensitivity C-reactive protein in patients with metabolic syndrome compared with healthy persons. In a cross sectional case control study, 150 patients with metabolic syndrome compared with 150 healthy persons enrolled. Body mass index, waist circumference, fasting blood glucose, blood pressure, lipids, and high-sensitivity C-reactive protein were measured. Metabolic syndrome was defined by According to guidelines from the National Heart, Lung, and Blood Institute and the American Heart Association. In this study, mean ± SD high-sensitivity C-reactive protein concentration in metabolic syndrome and in healthy persons were 2.44 ± 0.16 mg/dl and 1.69 ± 0.31mg/dl respectively so that there was significant difference between two groups (p=0.02). Sensitivity of high-sensitivity C-reactive protein in metabolic syndrome was 68% and other metabolic components were waist circumference 93%, blood pressure 98%, TG 81%, fasting blood glucose 98% and high density lipoprotein 21%. Sensitivity of high-sensitivity C-reactive protein in comparison with other components was significant. There was a significant close relationship between high-sensitivity C-reactive protein and metabolic syndrome components. This observation may in part account for the association of high-sensitivity C-reactive protein with markers of the metabolic syndrome. These data suggest that measurement of high-sensitivity C-reactive protein with other metabolic components have clinically important prognostic information and strong predictor of metabolic syndrome.*

**Key words:** High-sensitivity C-reactive protein**, metabolic syndrome, cardiovascular disease, diabetes mellitus

## INTRODUCTION

Metabolic syndrome comprises a cluster of abnormalities with insulin resistance and adiposity as central features.[1]According to guidelines from the National Heart, Lung, and Blood Institute and the American Heart Association, and the presence of any three features [central obesity, dyslipidemia (high triglycerides, low High Density Lipoprotein), hypertension, and impaired fasting glucose] is considered sufficient to diagnose the syndrome [1, 2]. Incidence of the metabolic syndrome is dependent on age, sex and geographical region [3]. In adults, it differs between 8% - 24% (males) and 7% - 43% (females).[3] Twenty-four percent of the US adults have the metabolic syndrome, and

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the prevalence increases with age (44% at age of 60 years) [4]. In Iran, the prevalence of metabolic syndrome is high (36%).[5,6] According to both criteria, the prevalence is higher in women than in men. An increasing trend is seen in both sexes [6].

There is a strong association between metabolic syndrome and the development of diabetes mellitus, cardiovascular disease [6]. Recent studies have suggested association between metabolic syndrome and inflammatory markers [7]. Abdominal obesity, especially a visceral fat, may play a key role in these situations because adipose tissue is known to have many hidden bioactive substances including inflammatory and anti-inflammatory proteins[8]. However, few studies have shown relationship between abdominal obesity and inflammatory changes that observed in metabolic syndrome [9]. High-sensitivity C-reactive protein influence metabolic syndrome and cardiovascular mortality and morbidity are related to it [8, 10].

The relationship between inflammatory markers and the traditional cardiovascular risk factor was strongly demonstrated [11]. Insulin resistance is the fundamental pathophysiological mechanism for development of metabolic syndrome[12], other factors such as proinflammatory cytokines (C-reactive protein, interleukin 6) and the relative anti-inflammatory adiponectin deficiency are also important [7, 13]. Metabolic syndrome can lead to heart disease, diabetes, and kidney damage [6]. The aim of this study was evaluating of association between components of metabolic syndrome and high-sensitivity C-reactive protein in patients with metabolic syndrome compared with healthy people.

## MATERIALS AND METHODS

Patients enrolled in the endocrinology clinics of Tabriz University of Medical sciences. According to guidelines from the National Heart, Lung, and Blood Institute and the American Heart Association metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions:

- Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension)
- Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia)

- HDL-C <40 mg/dL in men or <50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
- Waist circumference ≥102 cm in men or ≥88 cm in women.
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Exclusion criteria in this study were: cardiovascular diseases, psychiatric problems, acute illnesses, inflammatory or chronic infectious diseases, smoking, major surgery. One hundred and fifty patients with metabolic syndrome and 150 normal individuals who were equal in age and sex were selected. The study was confirmed by the institutional committee of ethical practice of the Tabriz University of Medical Sciences.

After an overnight fast, blood sample for fasting blood glucose, lipid profile and high-sensitivity C-reactive protein was collected. High-sensitivity C-reactive protein was measured by using an immunoturbidimetric assay.

### Statistical analysis

Statistical analysis was done by SPSS 21. The data is shown as Mean ± SD and 95% confidence interval. Normality of the distribution was checked for each variable (one sample Kolmogorov- Smirnov test). Independent T-test was used to check difference between the means of two groups. Sensitivity of factors was estimated by area under the ROC curve. The determination of correlation was carried out using Pearsons one-tailed bivariate model. Odd's ratio was calculated by logistic regression. Chi-square and Fisher's exact tests were used to determine statistical difference in qualitative variables. P value less than 0.05 was considered as statistically significant.

## RESULTS

In this study, the prevalence of metabolic syndrome was 32.1%, which was significantly higher in women than in males. One hundred and fifty patients with metabolic syndrome (72% women and 28% men) were selected. One hundred and fifty healthy persons, (68%) women and (32%) men enter the study. Demographical characteristics and metabolic components of the case and control groups are shown in table 1.

**Table 1: Demographical characteristics of the patients and control groups**

| Parameters | Case (n=150) | Control (n=150) | P Value |
|---|---|---|---|
| Sex male/female | 108/42 | 102/48 | 1.0 |
| Age (year) | 54.4±10.9 | 50.23±11.3 | 0.8 |
| waist circumference (cm) | 105.8±10.3 | 77.1±20.1 | 0.001 |
| HDL (mg/dl) | 42.3±9.8 | 52.7±12.9 | 0.02 |
| TG (mg/dl) | 202.2±11.1 | 115±9.4 | 0.001 |
| Blood pressure (mmHg) | 137/82 | 110/70 | 0.003 |
| FBS (mg/dl) | 168.1±4.3 | 88.8±8.9 | 0.002 |
| BMI (kg/m²) | 30±4.4 | 24.5±3.8 | 0.5 |

According to table 1, there was no difference between these two groups considering age and sex but obviously there was a significant difference in metabolic components between both groups.

The prevalence of metabolic syndrome increased with age and body mass index in both genders. In this study, the most common metabolic disorder was hypertriglyceridemia. Mean ± SD of high-sensitivity C-reactive protein in metabolic syndrome and control group was 2.44±0.16mg/dl and 1.69±0.31mg/dl respectively. So that a significant difference was observed between case and control groups (p=0.02). High-sensitivity C-reactive protein cut of point was 2 mg/L. According to this study, high-sensitivity C-reactive protein odd's ratio was 1.26 (95% CI, 1.09-1.54). High-sensitivity C-reactive protein levels have positive significant correlation with metabolic components (p=0.007, r=0.1) while it has a negative significant correlation with HDL (p<0.001, r=-0.2).There was no significant correlation between age and high-sensitivity C-reactive protein level.

Sensitivity of high-sensitivity C-reactive protein level in patients with metabolic syndrome was 68% (p<0.001). Graph 1 demonstrates the sensitivity of high-sensitivity C-reactive protein and other metabolic components.

According to the graph 2, all metabolic components were highly sensitive in metabolic syndrome patients (waist circumference 93%, triglyceride 82%, fasting blood glucose 91%, Blood pressure 90%) but HDL level had low sensitivity (21%) for the selected patients with metabolic syndrome.
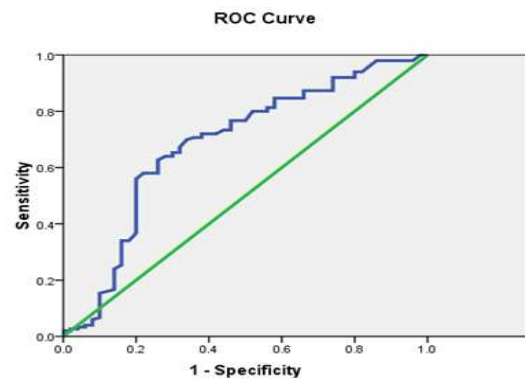


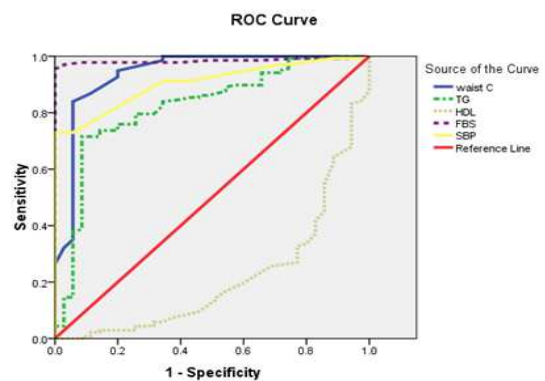**Figure 1 :sensitivity hs-CRP in prediction of metabolic syndrome**



**Figure 2. Sensitivity of five metabolic syndrome components in disease prediction**

## DISCUSSION

Metabolic Syndrome is a condition that represents a cluster of risk factors. People with metabolic Syndrome are much more likely to develop chronic health conditions, including cardiovascular disease and diabetes [14].
Metabolic syndrome seems to be a proinflammatory state characterized by increased concentrations of C-reactive protein.[13,14] Several earlier studies have shown that high C-reactive protein concentrations indicate the development of diabetes.[14] This study investigated metabolic syndrome and its association with high-sensitivity C-reactive protein levels. More studies detected a highly significant association between plasma levels of C-reactive protein and severity of carotid stenosis or other cardiovascular diseases [15]. This study discloses that high-sensitivity C-reactive protein is significantly increased in patients with metabolic syndrome. We found that sensitivity of high-sensitivity C-reactive protein was higher than other metabolic components. The results of this

study were consistent with other studies. All components of metabolic syndrome were significantly associated with level of high-sensitivity C-reactive protein. Measuring high-sensitivity C-reactive protein in the metabolic syndrome may be helpful for prediction of early stages of cardiovascular diseases.

Data of clinical series support the idea that high-sensitivity C-reactive protein is associated with total and abdominal adiposity, metabolic syndrome and its components [13,16], Similar to our study, Oliveira et al shown high-sensitivity C-reactive protein were higher in metabolic syndrome and high-sensitivity C-reactive protein is strongly related with metabolic syndrome and its components.[17] Body mass index was the best predictor of high-sensitivity C-reactive protein and hypertriglyceridemia was also related to this inflammatory marker [18].

Moreover, the association between hypertension and high-sensitivity C-reactive protein may reflect endothelial dysfunction [19]. Abdominal obesity may exhibit distinct effect on inflammatory and anti-inflammatory proteins and modulate inflammatory network in metabolic syndrome [19].

In previous studies, positive correlations were found between levels of C-reactive protein and fasting blood glucose, triglycerides and body mass index and negative correlations were found with HDL cholesterol [20, 21]. A linear increase in C-reactive protein along with increasing of abnormal metabolic features was also observed in previous studies [22]. Similar in our study, Santos et al was shown high-sensitivity C-reactive protein was significantly correlation with metabolic syndrome components independent of sex, age and smoking status [23]. He reported high-sensitivity C-reactive protein level was more than 2.4 mg/dl in patients with waist circumference more than 102 cm in men and 88 cm in women[23].

In our study, we found higher level of high-sensitivity C-reactive protein in metabolic syndrome and significant positive relationship between components of metabolic syndrome and high-sensitivity C-reactive protein. In our study, all components of the metabolic syndrome are associated with high-sensitivity C-reactive protein, regardless of age and sex and in this study, it was found that components of the metabolic syndrome, such as high-sensitivity C-reactive protein, could predict metabolic syndrome**.** Regard of our study screening of metabolic syndrome seems to be important because we can predict subsequent development of diabetes and cardiovascular diseases. It is best to consider high-sensitivity C-reactive protein as a predictor of metabolic syndrome.

## CONCLUSION

This study shown patient with metabolic syndrome has higher levels of high-sensitivity C-reactive protein and it is strongly associated with metabolic syndrome and its components. High-sensitivity C-reactive protein is useful biomarkers in prediction of metabolic syndrome and it is superior to measure its level in these patients to predict cardiovascular problems. According to this study and other studies, high-sensitivity C-reactive protein as a new arrangement for the diagnosis of metabolic syndrome should be considered.

### Conflict of interest
The authors declare that they have no competing interests.

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