HIGH SENSITIVITY C-REACTIVE PROTEIN (HS-CRP) AND METABOLIC SYNDROME: CORRELATION WITH NUMBER AND TYPE OF METABOLIC SYNDROME COMPONENTS IN IRAQI PATIENTS

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ABSTRACT

Background: **Metabolic syndrome (MetS) is clustered risk factors that arise from insulin resistance and is associated with risk of coronary heart disease, as well as diabetes. American Heart Association (AHA) defined MetSon the basis of 5 components: fasting blood glucose, blood pressure, triglycerides, HDL-C, and waist circumference. High-sensitivity CRP (hs-CRP) is a measure of systemic inflammatory conditions and is considered as a risk factor in diabetes mellitus.**

Aim: **To investigate the correlation of hs-CRP with the number and type of components of MetS diagnostic criteria in Iraqi patients and to find out the cutoff point for hs-CRP level that might predict the development of metabolic syndrome.**

Methods: **This study involved 78 diabetic patients consulting the outpatient clinic at Al Sadr Teaching Hospital. For all patients anthropometric measures were obtained and fasting blood samples were taken for determination of blood glucose, lipid profile and hs-CRP level.**

Results: **Mets was diagnosed in 48 patients. The level of hs-CRP was found to be significantly increased with increasing number of components of MetS. The lowest value of (0.07 mg/dl) was found in people with absent components of metabolic syndrome and the highest level of (4.05 mg/dl) in subjects with 4 components. A significant positive correlation was observed between hs-CRP and waist circumference, FBG, and triglycerides(r=0.514, 0.531, 0.592 respectively, P<001) and a negative correlation with HDL-cholesterol (r=-0.332, p=0.021). Using the level of 0.65 mg/dl, hs-CRP can predict the development of metabolic syndrome with sensitivity and specificity of 81.3% and 93.3% respectively.**

Conclusion: **Hs-CRP shows a significant correlation with the number of MetS components and its level correlates well with waist circumference and other biochemical features of MetS. Hs-CRP can predict the development of MetS with high sensitivity and specificity.**

INTRODUCTION

Metabolic syndrome (MetS) is a cluster of risk factors that arises from insulin resistance accompanying abnormal adipose deposition and function, and is associated with risk of coronary heart disease, as well as diabetes, fatty liver, and several cancers.[1-4] In 2005, National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA) defined MetS when a patient has at least 3 of the following 5 conditions;[4] fasting glucose ≥100 mg/dl, blood pressure ≥130/85 mm Hg, triglycerides ≥150 mg/dl, HDL-C < 40 mg/dl in men or <50 mg/dl in women, waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women. High sensitivity C reactive protein (hs-CRP) is reported to be a measure of systemic inflammatory condition and is considered as a risk factor in cardiovascular diseases and diabetes mellitus.[5] hs-CRP has also been linked to the MetS.[6-8] In 2006, a consensus group of the International Diabetes Federation (IDF) issued an updated definition of the MetS and also recommended further research into additional criteria that should be part of the definition of the MetS to improve its strength and validity in predicting outcomes.[9]

In this study, the correlation between hs-CRP and the number and type of components of MetS diagnostic criteria in Iraqi patients is investigated. In addition, the study aims to find out a cutoff point for the level of hs-CRP that can predict the development of MetS.

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PATIENTS AND METHODS

The study was carried out at Al Sadr Teaching Hospital, in Basrah province. It involved78diabetic patients consulting the outpatient clinic. In all the study group, anthropometric measurements were done, blood pressure determined and venous blood samples were collected for measuring fasting blood glucose (FBG), serum triglyceride and HDL-cholesterol and hs-CRP. Blood glucose was determined using glucose kit (Gluco-PAP) supplied by RANDOX Laboratories Ltd, United Kingdom, in which glucose was determined after enzymatic oxidation in the presence of glucose oxidase. Serum triglyceride level was determined using triglyceride kit (GPO–method) supplied by BIOLABO REAGENT, France, in which triglyceride level was determined using Fossati and Prencipe method associated with Trinder reaction.[10] HDL-cholesterol was also determined in samples after precipitation of low density lipoprotein, very low density lipoprotein and chylomicron using phosphotungestic acid (PTA) and magnesium chloride. The HDL-cholesterol obtained in the supernatant after centrifugation was then measured using cholesterol reagent (cholesterol CHOP-PAP) supplied by BIOLABO REAGEN, France. Hs-CRP was determined using a ccubindelisa kit supplied by Monobind Inc., USA based on sandwich immunoenzymatic assay.

Statistical analyses were made using analysis of variance (ANOVA), Student's t-test, and correlation coefficient (r). P-value <0.05 was considered statistically significant. Receiver-operating characteristic (ROC) curve analysis for diagnosing MetS was performed to obtain the area under ROC curve (AUC) and an optimal cutoff point of hs-CRP for diagnosing MetS. An optimal cutoff point was defined as the point on a ROC curve nearest to the point where both sensitivity and specificity were 1. All data were analyzed with SPSS software (statistical Package for the Social Sciences, version 15.0 for windows XP; SPSS, Inc, Chicago).

RESULTS

Among 78 diabetic patients enrolled in this study, 48 fulfilled the diagnostic criteria of metabolic syndrome based on American Heart Association definition.[5] The anthropometric and biochemical characteristics of those with and without metabolic syndrome are shown in (Table-1). There is a significant statistical difference in FBG, triglycerides, HDL, waist circumference and waist/hip ratio between the two groups with P value <0.05.

Table 1. Anthropometric and biochemical characteristics of the study group with and without MetS.

	MetS (N=48)	NoMetS (N= 30)	P value*
Age (yrs)	54.4(± 12.4)	58.0 (±9.7)	0.194
Waist circumference(cm)	104.7 (±10.7)	90.5 (±10.2)	<0.001
Waist/Hip ratio	.98 (±0.07)	.82 (±0.11)	<0.001
Systolic blood pressure (mmHg)	147.6 (±18.4)	130.0 (±11.5)	0.383
Diastolic blood pressure (mmHg)	89.7 (±9.02)	83.1 (±8.1)	0.013
FBG (mg/dl)	189.2 (±66.3)	118.6 (±59.9)	<0.001
Triglycerides (mg/dl)	208.3 (±104.6)	120.1 (±40.1)	<0.001
HDL (mg/dl)	39.7 (±11.3)	46.7 (±19.8)	<0.001
Hs-CRP (mg/dl)	2.13 (±1.8)	.30 (±0.21)	<0.001

Data are expressed as mean ± SD.
****P< 0.05 was considered statistically significant***

The level of hs-CRP was found to be gradually increased with increasing number of components of MetS with the lowest level of (0.07 mg/dl) found in people with absent components of the metabolic syndrome and the highest level of (4.05mg/dl) in subjects with four components of the MetS. These differences are statistically significant (P- value <0.05).

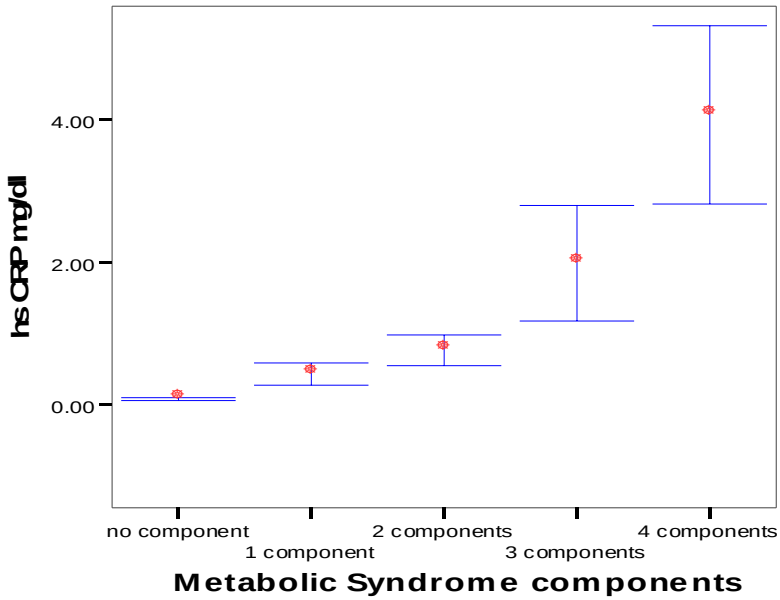

Fig 1. The level of hs-CRP according to the number of components of metabolic syndrome

(Error bars show 95% CI of the mean)

The level of hs-CRP correlates with the type of components of MetS, with a significant positive correlation observed between waist circumference, FBG, and triglycerides (r=0.514, 0.531, 0.592 respectively, P=<001),a negative correlation with HDL-cholesterol (r=-0.332, P=0.021), and no significant correlation with both systolic and diastolic blood pressures (r= 0.054,P=0.73;r=0.21,P=0.16).When selecting hs-CRP of 0.65 mg/dl as a cutoff point for predicting the development of MetS,[11] it was found to have a sensitivity of 81.3% and a specificity of 93.3% with positive predictive value of 95.1% and negative predictive value of 75.7%. Figure-2 shows the Receiver Operating Characteristic Curve (ROC) for hs-CRP in patients with metabolic syndrome with an area under curve of 0.946.

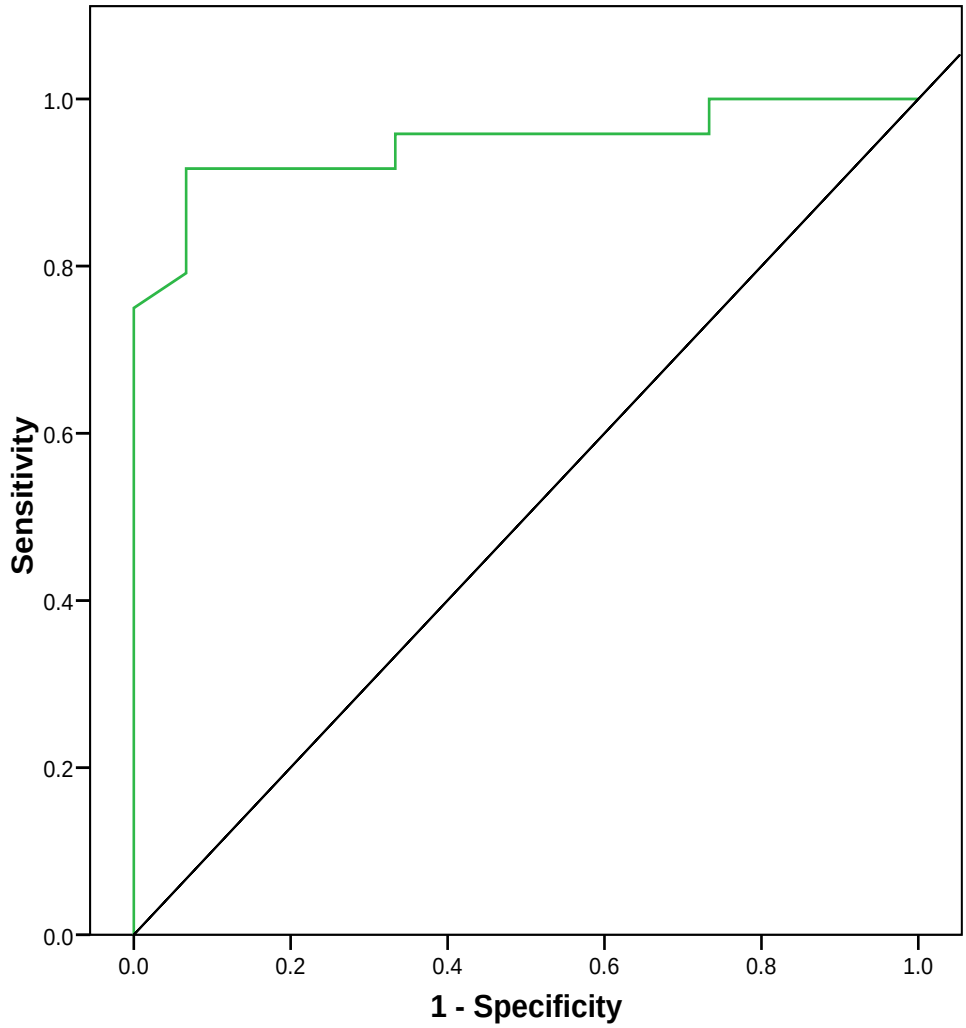

Fig -2- Receiver Operator Characteristic (ROC) curve for hs-CRP in patients with metabolic syndrome

DISCUSSION

Metabolic syndrome comprises a cluster of abnormalities with insulin resistance and adiposity as central features. Low-grade inflammation has been hypothesized to be involved in the pathogenesis of MetS.[12] As this study demonstrated, high levels of hs-CRP were observed in patients with metabolic syndrome. This was supported by the study of Ridker et al. that showed CRP levels to be elevated in patients with the MetS.[13] The present study found a significant correlation between hs-CRP and waist circumference which was supported by work of Ouchi, et al. [14] who confirmed the expression of CRP mRNA in human adipose tissue, and that adipose tissue is an important source for circulating CRP. This correlation is further supported by the study of Festa, et al.[15]that showed strong association between CRP levels, central adiposity, and insulin resistance. Cytokine production by adipocytes might mediate the elevation of CRP levels. Adipose tissue secretes a number of cytokines, among which is interleukin 6 (IL-6) which regulates hepatic production of CRP.[16] The significant positive correlation between hs-CRP and fasting blood glucose could be attributed to the role of hs-CRP in insulin signaling. Xu, et al[17] showed that recombinant CRP attenuates insulin signaling through the regulation of spleen tyrosine kinase, mitogen-activated

protein kinase, insulin receptor substrate-1, and endothelial nitric oxide synthase in vascular endothelial cells. The effects of human recombinant CRP (hr-CRP) on insulin signaling involved in glucose transport are mediated by increasing insulin receptor substrate-1 phosphorylation leading to impaired insulin-stimulated glucose uptake and glucose transporter.[18] In accordance with others,[19] the present study demonstrated that hs-CRP levels were positively correlated with triglycerides level. It is suggested that this unfavorable lipid profile may facilitate the formation of foam cells in the arterial wall, increasing the inflammatory activity.[20] Although IDF consensus on updating the criteria of diagnosing MetS, there is still controversy on the use of hs-CRP as component in diagnostic criteria. Compared with Oda et al who found the sensitivity =65% and specificity =62.6%,[21,22] the present study demonstrated higher sensitivity and specificity (81.3%, 93.3% respectively).

In conclusion, this study demonstrated that hs-CRP showed a significant association with the number of MetS components and its level correlated well with waist circumference and other biochemical features of MetS. Adopting a level of 0.65 mg/dl, hs-CRP can predict the development of metabolic syndrome with sensitivity and specificity of 81.3%, 93.3% respectively.

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