



C - reactive protein in relation to fasting glucose levels in obese or overweight men

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Abstract

C-reactive protein (CRP) as an inflammatory cytokine is associated with insulin resistance, obesity and type II diabetes. The purpose of this study was to examine the relation of CRP to glucose concentration in adult obese or overweight men and to compare this inflammatory cytokine between normal weight and obese or overweight men. Participants included fourteen non athletes sedentary overweight or obese ($30 \leq \text{BMI} \leq 36$) and ten normal weight ($20 \leq \text{BMI} \leq 26$) men aged 34 – 41 year. Fasting blood samples were taken after an overnight fast to determine glucose, insulin, and C - reactive protein in two groups. Independent T test used to compare all variables between two groups and Pearson correlation method was used to relation between them. Fasting serum CRP concentrations were higher in obese or overweight subjects than in normal weight men (2205 ± 805 versus 375 ± 181 ng/ml, $P = 0.005$). Serum CRP was positively related with glucose concentration in obese group ($p = 0.001$, $r = 0.77$). Based on these finding, we can say serum CRP affect directly glucose concentration in obese individuals.

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Introduction

C-reactive protein is a key inflammatory factor produced by the liver in response to acute infection or inflammation and its plasma concentration can increase up to 1000 times in response to injury or infection (Schultz *et al.*, 1990). CRP is synthesized mainly by hepatic ducts and regulated by IL-1b, IL-6 and TNF- α . CRP is known to be a better indicator than other cytokines in predicting cardiovascular disease (Nicklas *et al.*, 2005). Most studies consider measurement of CRP the only factor for identification of inflammation; however, measuring other inflammatory markers, along with CRP provides better information about the mechanisms involved in inflammation (Julia *et al.*, 2010). The US Center for Disease Control and Prevention describes CRP as the most important clinical marker useful in understanding inflammation and evaluating cardiovascular disease risk factors (Pearson *et al.*, 2003). Increased CRP and its connection to LDL and vLDL are known to lead to inhibit blood coagulation. In fact, these studies support the anti-blood-clotting property of CRP (De Ferranti *et al.*, 2002). Previous sources suggest that reduced CRP induced by weight loss is associated with increased serum adiponectin levels (Ouchi *et al.*, 2003).

Higher levels of this anti-inflammatory cytokine are associated with with coronary artery disease, obesity, diabetes, smoking and sedentary lifestyles (Bruun *et al.*, 2003). Studies on large numbers of men and women indicate that along with age, hypertension and diabetes, CRP is considered to be the most important factor for CVD (Panagiotakos *et al.*, 2008). Its association with dietary fibers and CRP concentration has also been reported previously (King *et al.*, 2005). Findings of another study showed that consumption of soy protein significantly decreased plasma levels of CRP compared with the placebo group (Azadbakht *et al.*, 2008). Clinical and epidemiological studies over the past decade indicate the negative relationship between CRP and adiponectin (Kantartzis *et al.*, 2006).

It is clear that in those with less physical activity baseline levels of CRP increase as a result of such mechanisms as increased oxidative stress or decreased insulin sensitivity (Pedersen, 2006). Scientific sources support higher levels of both glucose and CRP as well as insulin resistance in obese populations and metabolic diseases associated with obesity (Ouchi *et al.*, 2003; Bruun *et al.*, 2006). However so far, the molecular mechanisms of the relationship between them in obese individuals are less known. In this study the relationship between CRP and fasting glucose levels and insulin resistance will be measured. Also the levels of the said variables between the two groups of overweight or obese men with normal weight individuals are also compared.

Subjects and methods

Participants included fourteen non athletes sedentary overweight or obese ($30 \leq \text{BMI} \leq 36$) and ten normal weight ($20 \leq \text{BMI} \leq 26$) men aged 34 – 41 year. Main objective of present study was to determine relationship between serum CRP and glucose concentration in obese men.

Inclusion and exclusion criteria

Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. The exclusion criteria were infections, renal diseases, hepatic disorders, use of alcohol, current medications, and symptoms of diabetes, hyperlipidemia, hypertension, coronary artery disease, and cerebrovascular disease.

Anthropometrical measurements

After introduction and awareness of the subjects of the objectives of the study and once they had completed consent forms, the process of test implementation began. The weight and height of the participants were measured by the same person when the participant had thin clothes on and was wearing no shoes. Body mass index (BMI) was calculated by dividing body mass (kg) by height in metres squared (m^2). Waist circumference and hip circumference

were measured in the most condensed part using a non-elastic cloth meter. Waist-to-hip ratio was calculated as abdominal circumference divided by hip circumference as measured to the nearest 0.5 cm with a standard measuring tape. All of these measurements were conducted by the same researcher. Percentage body fat was measured using body composition monitor (OMRON, Finland). Each of these measurements was conducted two times and the average was reported. Resting blood pressure (BP) levels were measured in the right arm with a cuff sphygmomanometer after a participant had been resting for 10 min.

Clinical measurements

Basal, fasting blood samples were taken after an overnight fast to determine glucose, insulin, and C - reactive protein in two groups. Blood was drawn from the antecubital vein. Sera, separated immediately after centrifugation with 3000 x g for 10 min, were stored at -70 °C until biochemical analyses were

performed. Serum CRP was determined by ELISA method (Diagnostics Biochem Canada Inc. High sensitivity C - reactive protein (Hs-CRP)). The Intra-assay coefficient of variation and sensitivity of the method were 5% and 10 ng/mL, respectively. Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran).

Statistical Analysis

Data were expressed as individual values or the mean ± SD for groups. Normality of distribution was assessed by Kolmogorov-Smirnov test. Independent student t test was used for between groups comparison. Pearson’s correlation coefficients were used to evaluate the correlations between serum CRP and glucose concentration in obese men.

Results

Experimental data are presented as means ± SD. Anthropometrical characteristics of obese and normal groups are showed in table 1 and 2.

Table 1. Characteristics of the obese subjects according to anthropometrical measurements.

	N	Minimum	Maximum	Mean	Std. Deviation
Age (year)	14	34	41	38.21	2.119
Height (cm)	14	162	176	173.00	4.224
Weight (kg)	14	79	105	94.71	7.194
Abdominal (cm)	14	96	112	104.86	4.639
Hip (cm)	14	98	114	106.07	4.714
WHO	14	.97	1.02	.9887	.01613
BMI (kg/m ²)	14	30	34	31.61	1.563
Body fat (%)	14	30	37	32.65	2.008

Table 2. Characteristics of the normal subjects according to anthropometrical measurements.

	N	Minimum	Maximum	Mean	Std. Deviation
Age (year)	10	35	39	37.60	1.360
Height (cm)	10	169	174	171.10	1.663
Weight (kg)	10	65	70	67.50	1.581
Abdominal (cm)	10	84	91	87.40	2.716
Hip (cm)	10	90	98	94.80	2.658
WHO	10	.88	.97	.9230	.04719
BMI (kg/m ²)	10	22	23	23.05	.232
Body fat (%)	10	21	23	21.83	.879

Fasting serum CRP concentrations were higher in obese men than in normal weight men (2205 +/- 805 versus 375 +/- 181 ng/ml, P = 0.005). Glucose concentration was significant higher in obese men than normal subjects (91.05 +/- 12.4 versus 84.9 +/- 12.5 ng/ml, P = 0.041). We have observed that in obese men the insulin resistance in serum were

significantly higher than in normal men (4.65 +/- 2.05 versus 3.12 +/- 0.57 ng/ml, P = 0.011).

Serum CRP is strongly and positively associated with fasting glucose in obese subjects (p = 0.001, r = 0.77, Fig 1). Serum CRP concentration was also positively related to insulin resistance (p = 0.025, r =

0.53). But, there was no correlation between serum CRP concentration and insulin concentration in these subjects ($p = 0.088$, $r = 0.38$).

Discussion

In confirmation of most previous studies, also in the present study comparison of the serum levels of CRP between obese and normal weight groups showed that obese men tend to have higher levels of this inflammatory cytokines than men of normal weight. The present findings indicate its 6-time higher levels in obese men than in men of normal weight. Increased CRP protein in blood circulation is associated with increased risk of cardiovascular disease, myocardial infarction, ischemic attack, type 2 diabetes and other disorders related with metabolic syndrome (Das *et al.*, 2001). Scientific studies suggest increased levels of CRP in obese populations compared with normal weight individuals (Cook *et al.*, 2000). Furthermore an inactive or sedentary lifestyle model directly or indirectly affects the circulatory CRP levels independently of obesity (Fishcher *et al.*, 2007).

The baseline CRP levels are at almost 40 percent governed by genetic and hereditary characteristics (Subodh *et al.*, 2005). It has been suggested that increased levels of CRP are associated with 2 to 5 times increase in the incidence of cardiovascular disease and type 2 diabetes (LaMonte *et al.*, 2002). Based on the findings of this study, it seems that the 6-time higher levels of it in obese men compared with men of normal weight, is not only because of obesity but also rooted in an inactive life style in the period prior to the study. According to extensive studies, CRP is as one of the most important predictor indicators of cardiovascular disease (Subodh *et al.*, 2005) and more recently it has been described as the most powerful predictor indicator of cardiovascular risk factors and mortality caused by them (Tice, 2003). Accordingly in a recent study after age matching, smoking, blood pressure, levels of CRP are far better predictors of CRP in prediction of LDL cardiovascular disease (Ridker,

2002).

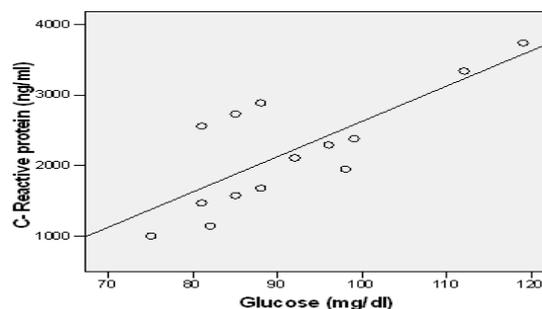


Fig. 1. The correlation pattern between serum CRP and glucose concentration in obese studied subjects.

Although some studies report no significant association between levels CRP and LDL, they propose simultaneous measurement of the two to diagnose or determine the intensity of cardiovascular disease (Ebrahim *et al.*, 2012). Although the pathophysiological mechanisms of insulin resistance and impaired insulin secretion representing the determinants of type 2 diabetes are not yet fully known, clinical studies are indicative of the pivotal role of inflammatory markers such as CRP in the pathogenesis of diabetes and insulin resistance (Pradhan *et al.*, 2001). In this connection clinical studies suggest that CRP and IL-6, two sensitive physiological markers of systemic inflammation are associated with hyperglycemia, insulin resistance and type 2 diabetes (Festa *et al.*, 2000; Frohlich *et al.*, 2000).

In recognition of the foregoing, the findings of this study also showed a direct and significant correlation of CRP levels and fasting glucose. These findings somehow support a concomitant increase in glucose and CRP in obese men. Based on research evidence, increased insulin resistance in obese compared to normal weight populations conventional significantly contributes to blood glucose differences between them. It is also possible that the increase in blood glucose in obese populations or obesity related-metabolic diseases is the result of a kind of relationship between higher levels of CRP and insulin performance. In response to the hypothesis, the findings of this study indicate a direct and significant

correlation between serum levels of CRP and insulin resistance in the research the population.

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