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Relationships between human serum C reactive protein, glucose concentration and insulin sensitivity in obese or overweight women

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Abstract

C-reactive protein (CRP) as an inflammatory marker is known to be a risk marker associated with cardiovascular diseases. In this study, relationship between serum CRP with glucose and insulin sensitivity were determined in obese or overweight women. For this purpose, fasting blood samples were collected in 21 sedentary healthy obese or overweight women (age, 39 ± 5.3 year; BMI, 32 ± 3.7 kg/m2) in order to measuring serum CRP, insulin and glucose concentration. Insulin sensitivity was calculated using insulin and glucose. Pearson's correlations were performed to identify possible relationship among the assessed variables. A positive association was observed between fasting glucose and serum CRP ($p = 0.027$, $r = 0.48$). There were no correlations between serum CRP concentrations with insulin ($p = 0.881$, $r = 0.035$) or insulin sensitivity ($p = 0.821$, $r = 0.053$). Our findings indicate that circulating CRP can be affect glucose concentration independent of insulin sensitivity in obese or overweight subjects.

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Introduction

In recent years obesity and overweight is increasing and expanding, and today it is considered one of the most serious public health problems in advanced societies and the developing. On the other hand, the literature regards obesity as a background for spread of development of some chronic diseases such as cardiovascular disease, metabolic syndrome, diabetes or diseases associated with insulin resistance.

Higher adiposity and obesity is associated with low-grade chronic inflammation and increased levels of pro-inflammatory cytokines and inflammatory markers, such as C-reactive protein (CRP). The levels of CRP are positively related to body mass index (BMI) (Panagiotakos *et al.*, 2005). It has been established that high sensitivity. CRP has been reported to be a strong and independent predictor of myocardial infarction, ischemic stroke, type 2 diabetes, and hypertension (Lindgarde *et al.*, 2004; Ridker, 2007). Reduced physiological response of peripheral tissues to the action of insulin named insulin resistance is one of the major causes of type 2 diabetes and plays a critical role in the pathogenesis of cardiovascular diseases (Deveci *et al.*, 2009). On the other hand, a large body of evidence suggests that obese subjects have higher glucose concentration or lower insulin sensitivity when compared with normal weight population (Chandalia *et al.*, 1999; Mahadik *et al.*, 2007).

A number of independent studies have indicated an association of elevated CRP concentrations in individuals with insulin resistance (Nakanishi *et al.*, 2005; Pradhan *et al.*, 2001). A large body of evidence has reported link inflammatory processes to impaired glucose metabolism (Ndumele *et al.*, 2006). On the other hand, raised C-reactive protein is a risk factor for type 2 diabetes (Hak *et al.*, 1999).

A reviewed of scientific studies suggest increased levels of CRP in obese or healthy individuals (Bruun *et al.*, 2003). However, increased blood glucose levels and reduced insulin sensitivity in obese diabetics or healthy obese individuals has been reported in previous studies. A close relationship of CRP with glucose and insulin resistance in diabetic patients has been observed before (Shoelson *et al.*, 2007; Kim *et al.*, 2007; Hotamisligil, 2006). But few studies have been conducted on establishing the relationship between glucose homeostasis and systemic levels of CRP in obese healthy subjects. Hence, this study aims to determine the relationship between blood glucose levels and insulin sensitivity in a small population of obese or overweighed healthy Iranian women.

Method and subjects

Subjects were twenty one sedentary adult obese or overweight women aged 38.9 ± 5.3 and BMI of 32 ± 7.4 kg/m² that participated by accessible sampling in this study. All subjects were non-smokers and non pregnancy. All participants had not participated in regular exercise/diet programs for the preceding 6 months. Subjects with a history or clinical evidence of impaired fasting glucose or diabetes, recent heart failure, active liver or kidney disease, or who were on medications known to alter insulin sensitivity were excluded. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form. All subjects had a body mass index (BMI) between 26 - 36 kg/m².
Anthropometrical and clinical measurements.

All anthropometric measurements were made by the same trained general physician. Body weight and height were measured on the same day to the nearest 0.1 kg and the nearest 0.1 cm, respectively. Body mass index was calculated from the weight and height measures. Percentage of body fat and visceral fat was estimated by bioelectrical impedance method (Omron Body Fat Analyzer, Finland). Abdominal obesity was determined as waist circumference measured in a standing position. Hip circumference was measured at the maximum circumference between the iliac crest and the crotch while the participant was standing and was recorded to the nearest 0.1 cm.

After anthropometrical measuring, all subjects were asked to attend laboratory after an overneight fast for blood sampling. Fasting blood samples were collected between 8 a.m to 9 a.m in order to measuring serum CRP, insulin and glucose. Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran). Serum CRP and insulin were determined by ELISA method. Depending of the values of insulin and glucose insulin sensitivity index (HOMA- IS) was calculated using the HOMA Calculator computer program (Katz *et al.*, 2000).

Statistical analysis

All values are given as mean and standard deviation. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. Statistic analysis was done with SPSS 15.0 for Windows. Pearson's correlation coefficient method used for determine serum CRP relations with glucose, insulin and insulin sensitivity. P>0.05 was considered as non-significant.

Results

As mentioned above, in this study we determined serum CRP relation with glucose and insulin sensitivity in non-trained obese or overweight women. Anthropometrical and clinical characteristics are showed in table 1. Data were expressed as individual values or the mean ± SD for groups. Data of Pearson's correlation coefficient showed tat serum CRP was associated negatively with fasting glucose concentration in studied subjects (p = 0.027, r = 0.48 , Fig 1). On the other hand, based on these data we can say serum CRP is a precise pro inflammation marker for glucose range in these subjects. In contrast, we did not significant correlation between serum CRP and insulin sensitivity in studied subjects (p = 0.821, r = 0.053, Fig 2). Also, there was no evidence that serum CRP was associated with serum insulin in studied subjects (p = 0.881, r = 0.035).

Table 1. Anthropometric and clinical characteristics of the study participants.

	N	Minimum	Maximum	Mean	Std. Deviation
Age	21	28	50	38.90	5.328
Height	21	152	172	161.14	5.642
Weight	21	67	113	83.50	10.270
Abdominal	21	97	130	110.45	9.985
Hip	21	97	128	113.86	8.696
WHO	21	.80	1.08	.9719	.06653
BMI	21	27	42	32.17	3.742
%fat	21	36	54	44.83	4.239
Visceral Fat	21	6	13	8.57	1.502
Glucose	21	76	114	92.05	9.341
Insulin	21	1.80	18.80	6.8857	4.51766
Insulin Resistanc	21	.42	4.50	1.5600	1.05429
Insulin sensitivity	21	.50	1.03	.7114	.14578

Discussion

Although the chief pathophysiologic mechanisms leading to insulin resistance or impaired insulin sensitivity and blood glucose levels in people with obesity and diabetes are not yet fully understood, it appears that inflammatory markers have major importance in this phenomenon. The key finding of this study is the close and significant relationship between levels of fasting glucose and CRP. These findings in fact indicate that higher levels of serum CRP in obese individuals lead to increased blood glucose and measurement of either of them introduces circulating levels of the other one. Moreover, despite a significant close relationship between glucose and CRP, the relationship between levels CRP and insulin sensitivity was linear but not significant. In support of these findings, some clinical studies support a close relationship and the role of

CRP and other inflammatory markers such as IL-6, in hyperglycemia phenomenon (Festa *et al.*, 2000; Frohlich *et al.*, 2003).

Preliminary human studies demonstrated that central obesity is a risk factor for decrease in insulin sensitivity, although the molecular mechanisms for this are less understood (Sujata *et al.*, 2010).

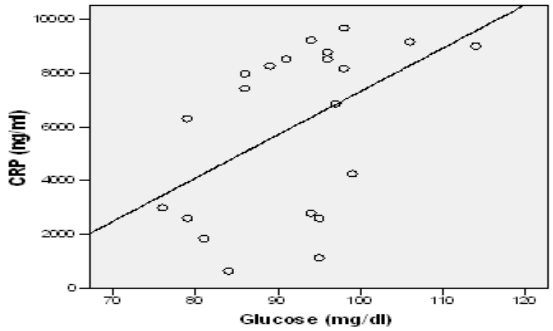

Fig. 1. Correlation coefficient between serum CRP and fasting glucose in studied subjects.

Obesity has been associated with elevated levels of CRP as an inflammation marker and predictor of cardiovascular risk (Choi *et al.*, 2013). Recent epidemiologic studies have demonstrated associations of elevated serum levels of C-reactive protein (CRP) with obesity, visceral adiposity, and insulin resistance, suggesting that a chronic inflammatory state is associated with hyperglycemia and diabetes through obesity or increased insulin resistance (Pradhan *et al.*, 2003; Wexler *et al.*, 2005; Laaksonen *et al.*, 2004).

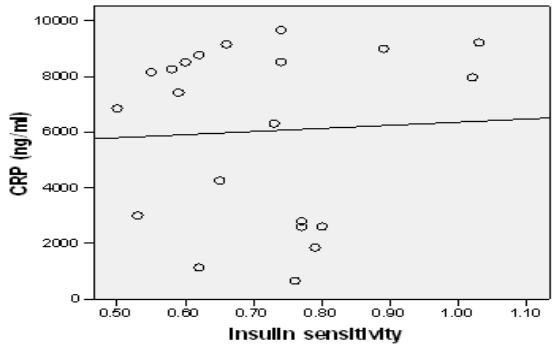

Fig. 2. No Correlation between serum CRP and insulin resistance is present in this Fig in.

Previous studies have concluded that along with age, hypertension and diabetes, CRP is the most important factor for CVD in this population (Panagiotakos *et al.*, 2008). In this context, recent sources report a kind of relationship between dietary fiber and serum CRP (King *et al.*, 2005). As to the importance of this inflammatory cytokine, American Heart Association and the Center for Disease Control and Prevention in the United States, have introduced CRP as the most important and most useful clinical marker in identification of inflammation and assessment of cardiovascular risk factors (Pearson *et al.*, 2003).

In the present study, despite a significant and close correlation between the serum levels of CRP and blood glucose in obese subjects, there was no significant relationship between insulin sensitivity and this inflammatory marker. Indeed, although most of the previous studies suggest decreased insulin sensitivity and increased levels of CRP in obesity or chronic diseases associated with obesity the study on overweighed or obese women showed that their patterns of changes are not correlated with each other in the presence of overweight or obesity. However, the reduced insulin sensitivity is one of the most important factors effective in the increase of blood glucose levels in healthy populations or patients. Based on these findings it can be concluded that CRP affects blood glucose levels independently of insulin sensitivity or performance. It is also likely that CRP affects or regulates blood glucose levels indirectly via other hormonal factors, or inflammatory and anti-inflammatory mediators, such as adiponectin, because previous literature support the significant inverse relationship of CRP with adiponectin as an anti-inflammatory cytokine (Kantartzis *et al.*, 2006). On the other hand, the close and meaningful relationship of adiponectin with blood glucose levels and insulin sensitivity has been frequently observed (Plaisance *et al.*, 2009; Ceddia *et al.*, 2005).

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