The correlation between serum high sensitivity c-reactive protein and leptin in reproductive age overweight/obese women in Erbil city

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Abstract

Background and objectives: Leptin could be a key regulator of C-reactive protein (CRP) levels, which serve as a marker of systemic inflammation. Both leptin and CRP are predictors of cardiovascular disease (CVD). This study, attempted to characterize the association between inflammatory marker hs-CRP and serum leptin in overweight/obese women in reproductive age in comparison with normal body mass index women (BMI) as a control group.

Methods: Eighty reproductive age women were divided into two groups: first group of 50 overweight / obese women; with mean age 27.7 years and BMI mean (31.4 Kg/m^2). The second group of 30 age-matched women with mean age 28.8 years and BMI mean (22.5 Kg/m^2) which served as control group. Any subject with other diseases or on medication that might affect the study was excluded. Fasting blood samples for both groups were collected and serum hs-CRP, leptin, lipid profile and glucose were measured

Results: In the overweight / obese group hs-CRP concentrations were significantly associated with BMI and leptin ($r = 0.3$, $r = 0.284$, with $p < 0.05$) respectively. This association remained significant, even after adjusting BMI, for each one unit increase in serum leptin the serum hs-CRP escalated by a mean of 0.05 (mg/L). Serum Leptin notably has a more significant role than BMI in explaining changes of serum hs-CRP since its standardized coefficient was higher (ß =0.384 with p=0.001) versus (ß =0.266 with p=0.016) for BMI in overweight and obese women.

Conclusion: Leptin is a stronger predictor of hs-CRP than BMI in overweight and obese women in reproductive age.

Keywords: High sensitivity C reactive protein, Leptin , Obesity, Body Mass Index

Introduction

Leptin, the adipocyte-derived protein product of the *ob* gene, is involved in appetite regulation and obesity through central effects at the hypothalamus. [1]

Leptin is related to the amount of body fat [2]. Leptin is also associated with increased heart rate , blood pressure, [3] and sympathetic neural activity, [4] and may contribute to platelet aggregation.[5,6]

Recent data have implicated leptin as an independent risk factor for cardiovascular diseases,[7,8,9] even after adjustment for traditional risk factors.[10] C reactive protein is synthesized by the liver and regulated by cytokines, especially interleukin (IL)-6.[11] The long form of the leptin receptor resembles the gp120 family of cytokine receptors, which includes the IL-6 receptor.[1,12] Both leptin and CRP may be increased in women, in obesity,[2] and in inflammation,[13,14,15] and both have been linked to cardiovascular pathophysiological processes and increased risk of (CVD).

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There is little information on any interaction between leptin and CRP, particularly in healthy normal subjects. This study showed the pertinent clinical relevance of leptin and CRP that both relate independently of the influences of gender, body mass index (BMI), and other variables

Methods

A sample of 80 women in reproductive age were divided into two groups: first group of 50 overweight / obese (26 overweight and 24 obese), they were aged between 20 to 39 years (mean 27.7 years) and BMI from 25 to 52.7 mean (31.4 Kg/m^2). The second group of 30 women, their ages ranged between 18 to 39 years old (mean 28.8 years) and BMI from 18.5 to 24.7 mean (22.5 Kg/m^2), served as control group. Subjects having clinical or electrocardiographic evidence of coronary artery disease, polycystic ovary syndrome, history of smoking or use of lipid lowering, anti-inflammatory medications or probable conditions which may provoke an inflammatory response were eliminated from the study. All Subjects attended the Rizgary Teaching Hospital in Erbil city.

After 12 hours fasting, blood samples in follicular phase for both groups (women were aware of the first day of their last menstrual cycle) were collected for determination of serum, hs-CRP, leptin, lipid profile and glucose.

Leptin hormone and hs-CRP were measured by a commercial ELISA kit Diagnostics Biochem (Canada Inc), serum glucose and lipid profile (after centrifugation at 3000 rpm for 5 minutes) were measured through enzymatic colorimetric assays.

Statistical analysis:

Statistical analysis were done using SPSS (Statistical Package for Social Sciences). The difference in mean between 2 groups was assessed by t-test.

Correlation coefficient was used to denote association between two quantitative variables and denoted by "r". A multiple linear regression model was used to assess the role of selected independent variables in explaining the changes in serum hs-CRP. Un standardized (partial regression coefficient): estimates the expected change in the level of response variable (measured in its units) as a net response to the effect of each independent variable included in the model, after controlling for the other explanatory variables included in the model. Calculated regression coefficient: reflects the statistical significance of the calculated standardized b (partial regression coefficient): Useful in ranking the explanatory variables in order of magnitude of effect on response variable. P value less than the 0.05 level of significance was considered statistically significant.

Results

Table (1) shows no statistically significant difference in the mean age between both study groups (28.8 years in control group and 27.7 years in overweight/obese women), while a statistically significant difference was observed for BMI in overweight and obese women group (31.4 Kg/m^2) in comparison to control group (22.5 Kg/m^2) with $p < 0.001$.

Table (2) shows statistically significant differences in the mean fasting serum concentrations for, hs-CRP, leptin, glucose, and triglyceride (5.1 mg/L, 35.4 ng/ml, 103.3 mg/dl and 118.7 mg/dl) respectively in overweight and obese group in comparison to the control group (2.8 mg/L, 16 ng/ml, 93.8 mg/dl, and 85.4 mg/dl) respectively.

The remaining biomarkers (VLDL-C, LDL-C, HDL-C and total cholesterol) showed no statistically significant differences between the two study groups.

Table (3) showed mean serum concentration of study biomarkers for 26 overweight and 24 obese cases categorized by BMI from 25 to 29.9 for overweight and 30 and over for obese .

There was generally no significant variation in the level of biomarkers investigated between overweight and obese women. The relationship between serum hs-CRP and leptin with other study biomarkers are

given in Table (4), a significant positive correlations were found between hs-CRP and each of BMI and serum leptin (r =0.3, r =0.284 ,with p <0.05) respectively, also significant correlation was found between serum leptin and BMI (r = 0.31 with p<0.05), while there were no significant positive correlation between each of hs-CRP and leptin with other study variable .

As shown in Table (5), a multiple linear regression model was used to assess the role of selected independent variables (BMI, serum leptin) in explaining the changes in serum hs-CRP .

Only BMI and serum leptin had a significant positive association and important role in explaining the magnitude of serum hs-CRP. For each one unit increase in BMI the serum hs-CRP increase by a mean of 0.13 (mg/L), after adjusting for serum leptin. For each one unit increase in serum leptin the serum hs-CRP increases by a mean of 0.05 (mg/L), after adjusting for BMI. Serum Leptin had a more important role than BMI in explaining changes in serum hs-CRP since its standardized coefficient was higher (ß =0.384 with p=0.001**)** versus (ß=0.266 with p=0.016) for BMI

Table 1: The difference in means of age and body mass index between the 2 groups**.**

	Controls (n=30)	**(Overweight/obese) (n=50)**	**P (t-test)**
Age in years			0.35[NS]
Range	(18 - 39)	(20 - 39)	
Mean ± SE	28.8±1.11	27.7±0.66	
BMI (Kg/m2)			<0.001
Range	(18.5 - 24.7)	(25 - 52.7)	
Mean± SE	22.5±0.3	31.4±0.77	

Table 2: Comparison between the two groups in mean of selected parameters

	Controls (n=30)	(Overweight/obese) (n=50)	P (t-test)
Serum hs- CRP (mg/L)			<0.001
Range	(0.2 - 8.8)	(0.3 - 9.7)	
Mean± SE	2.8±0.48	5.1±0.38	
Serum leptin (ng /ml)			<0.001
Range	(3.3 - 74.8)	(3.5 - 95.5)	
Mean± SE	16±3.35	35.4±2.62	
Serum fasting glucose (mg/dl)			0.01
Range	(75 - 127)	(72 - 140)	
Mean± SE	93.8±2.27	103.3±2.44	
Serum VLDL-C (mg/dl)			0.07[NS]
Range	(9 - 64)	(13 - 59)	
Mean± SE	19.9±2.15	24.7±1.6	
Serum LDL-C (mg/dl)			0.08[NS]
Range	(54 - 206)	(75 - 183)	
Mean± SE	105.6±6.83	117.3±3.13	
Serum HDL-C (mg/dl)			0.4[NS]
Range	(25 - 51)	(22 - 55)	
Mean± SE	38.3±1.76	36.7±1.09	
Serum Triglyceride (mg/dl)			0.01
Range	(40 - 230)	(26 - 290)	
Mean± SE	85.4 ±8.08	118.7±8.47	
Serum Cholesterol (mg/dl)			0.35[NS]
Range	(80 - 220)	(95 - 245)	
Mean± SE	158±6.73	149.9±5.36	

Table 3: Comparison in means of selected parameters between overweight and obese group categorized by BMI**.**

	Overweight (25-29.9 kg/m2) (n=26)	**Obese (30+kg/m2) (n=24)**	**P (t-test)**
Serum hs- CRP (mg/L)			0.13[NS]
Range	(0.3 - 9.7)	(0.3 - 9.2)	
Mean± SE	4.6±0.52	5.7±0.55	
Serum leptine (ng/ml)			0.1[NS]
Range	(4.9 - 65.1)	(3.5 - 95.5)	
Mean± SE	31.3±2.7	39.8±4.5	
Serum fasting blood glucose (mg/dl)			0.67[NS]
Range	(72 - 133)	(81 - 140)	
Mean± SE	102.3±3.53	104.5±3.43	
Serum VLDL-C (mg/dl)			0.89[NS]
Range	(13 - 59)	(14 - 48)	
Mean± SE	24.9±2.57	24.5±1.89	
Serum LDL-C (mg/dl)			0.37[NS]
Range	(75 - 183)	(82 - 156)	
Mean± SE	120±4.75	114.3±4.02	
Serum HDL-C (mg/dl)			0.22[NS]
Range	(24 - 55)	(22 - 51)	
Mean± SE	38±1.59	35.3±1.47	
Serum Triglyceride (mg/dl)			0.96[NS]
Range	(26 - 290)	(35 - 237)	
Mean± SE	118.3±13.79	119.3±9.7	
Serum Cholesterol (mg/dl)			0.2[NS]
Range	(105 - 245)	(95 - 210)	
Mean± SE	156.5±8.29	142.6±6.51	

Table 4: Linear correlation coefficient between hs-CRP and leptin with other study variable in overweight /obese group

	Serum hs-CRP	Serum leptin
Age in years	r=-0.08 P=0.58[NS]	r=0.036 P=0.8[NS]
BMI	r=0.3 P=0.034	r=0.31 P=0.028
Serum hs- CRP	***	r=0.284 P=0.045
Serum fasting glucose	r=0.062 P=0.67[NS]	r=0.008 P=0.95[NS]
Serum cholesterol	r=0.122 P=0.21[NS]	r=0.151 P=0.29[NS]
Serum VLDL-C	r=-0.195 P=0.18[NS]	r=-0.069 P=0.64[NS]
Serum LDL-C	r=0.147 P=0.31[NS]	r=0.178 P=0.22[NS]
Serum HDL-C	r=0.008 P=0.96[NS]	r=0.142 P=0.32[NS]
Serum Triglyceride	r=-0.121 P=0.4[NS]	r=-0.017 P=0.91[NS]
Serum leptin	r=0.284 P=0.045	

Table 5: Multiple linear regression model with serum hs- CRP (mg/L) as the dependent (response) variable and selected explanatory (independent) variables.

	Partial regression coefficient	P	Standardized coefficient ß
BMI (Kg/m2)	0.13	0.016	0.266
Serum leptine (ng/ml)	0.05	0.001	0.384

Discussion

To the best of our knowledge this is the first study in Kurdistan region to address the relationship between serum leptin concentrations and hs-CRP in overweight and obese women compared to healthy control group. Furthermore, only women are studied in order to be able to completely dispel the possibility of confounding effects due to gender-based differences. In addition, the blood tests were conducted only during the follicular phase of the menstrual cycle in order to obviate the possibility of estrogen-related effects on inflammatory markers and hs-CRP.[16] This study fills an important knowledge about the in *vivo* association between leptin and hs-CRP by the observation of significant positive correlation between serum leptin concentrations and hs-CRP and these markers with BMI in overweight and obese, but otherwise healthy control group individuals showed statistically significant lower serum leptin, hs-CRP and BMI .

The study finding corroborated the findings of others who reported a positive correlation between serum leptin and CRP concentrations.[17-19] All variables were entered into the study simultaneously tested for linear correlation coefficient, many of the variables included (age, lipid profile and serum glucose) were showed non significant correlation to serum leptin and hs-CRP therefore they were excluded from multiple regression analyses. The variable with significantly high standardized coefficient with the strongest effect on hs-CRP

than BMI was leptin. In this and other studies in apparently healthy women,[19,20] leptin predicted CRP levels independent of BMI, suggesting that adipose tissue only partially mediates the leptin-CRP association, and alternative pathways unrelated to general adiposity may be involved. For example, leptin may up regulate CRP levels by directly inducing interleukin-6 (IL-6) production [21] and by the leptin receptor, which has been shown to have intracellular signaling capabilities of IL-6-type cytokine receptors [12].

Study findings have limited contribution to the data available on the apparently healthy reproductive age women with > 25 kg/m ^{2} of BMI. The significant correlation between concentrations of leptin and CRP and the relationship between the highest concentrations of these biomarkers and significantly raised risk of developing CVD [22] might prove useful for risk stratification and assessment of prognosis in the general population particularly in the current population-based study focusing on women in reproductive age who showed few, if any, of the potential confounding factors that are frequently detected in older, diseased populations with hypertension, dyslipidemia, and insulin resistance, and might explain the suboptimal performance of CRP when used as a biomarker of cardiovascular risk in some studies.[23,10]

Conclusion

Leptin is a stronger predictor of hs-CRP than body mass index BMI, in reproductive age overweight and obese women

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