Investigating relationship between C- reactive protein and obesity in adults

Leila Jamshidi [1]   Simin Hojjatoleslami [1]

Deprtment of Nursing [1], Hamadan Branch, Islamic Azad University, Hamadan, Iran.

Original Article

Abstract

Correspondence:
Leila Jamshidi, MSc.
Department of Nursing,
Hamadan Branch, Islamic
Azad University.
Hamadan, Iran
Tel:+98 8134494152
Email:
jamshidi.leila@gmail.com

Introduction: Association between plasma high-sensitivity C-reactive protein (CRP) concentrations and cardiovascular disease has been Investigated. C-reactive protein (CRP) is an acute phase reactant which is a marker of inflammation in the body. CRP is made by the liver in response to inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNFα). Adipose tissue is a major source of these inflammatory cytokines. The purpose of this study was, to examine differences in high-sensitivity C-reactive protein (hs-CRP) levels and body fatness.

Methods: A total of 260 adult healthy men and women were investigated in 2014. Body mass index (BMI) was measured for each participant. Blood samples were collected and CRP measurements were performed in the laboratory. Plasma CRP levels were measured by means of a colorimetric competitive ELISA. Data are expressed as mean$\pm$SD values. Relationship between obesity and CRP was analyzed by SPSS 20, and tested using χ^2-test and logistic regression analysis.

Results: Subjects with elevated CRP had higher BMI and WC. For elevated CRP, subjects in the highest BMI quartile with subjects in the lowest BMI quartile. The result shows a relationship between CRP with BMI throughout the BMI spectrum. CRP levels were strongly correlated with BMI (P=0.0002).Levels of CRP also increased steadily across WC quartiles (P=0.0001). Waist circumference quartiles were also strongly associated with odds of elevated CRP. Women in the highest WC (91cm) and men in the highest WC (89cm) had an odd of elevated CRP.

Conclusion: Development and implementation of a global health strategy for prevention and control of non-communicable diseasesin recommended.

Key words: C- Reactive Protein, Obesity, BMI, Waist Circumference

Introduction:

Overweight and obesity are linked to more deaths worldwide than underweight. Raised BMI is a major risk factor for non-communicable diseases such as: cardiovascular diseases (mainly heart disease and stroke), which were the leading cause of death in 2012; diabetes; musculoskeletal disorders, some cancers. In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 600 million were obese. The worldwide prevalence of obesity more than doubled

between 1980 and 2014 (1). Some of this risk may be mediated by inflammatory pathways (2).

Recently, inflammation has been understood to be a key pathogenic mechanism in the initiation and progression of CVD (3), and great attention has been given to inflammatory markers for their ability to predict CVD risk (4). Among these, C-reactive protein (CRP) has emerged as a powerful marker. An association between plasma high-sensitivity C-reactive protein (CRP) concentrations and cardiovascular disease has been noted in both men and women. A recent meta-analysis (5) of 7 prospective epidemiologic studies has provided strong evidence that elevated plasma concentrations of CRP predict coronary heart disease (CHD).

Understanding this association is of great importance because it may provide new insight into mechanisms of atherosclerosis or thrombotic events as well as lead to potential new prevention strategies or therapeutic interventions (6). Numerous pathophysiological mechanisms linking obesity and cardiovascular risk have been postulated (7).

Subsequent studies have demonstrated that CRP concentrations are significantly related to various measures of body fat (6). In an individual participant meta-analysis, every 1-SD increase in CRP was shown to increase vascular risk by more than 60% (8) and in one8 of these studies, weight loss led to a fall in CRP concentrations (6). Still, few data regarding CRP and obesity types (central obesity and BMI) have been generated for minority populations. On the other hand, According to Tehran Lipid and Glucose Study after study on 30 provinces, Waist Iranian-sectional in men, Greater than 89 cm and women over 91cm were considered Obesity (9).

Therefore, the purpose of this study was, investigating relationship between-reactive protein and types of obesity (central and general) in adults.

Methods:

In this cross-sectional screening study , from a total of 300 employees, 260 men and women who were present at the time of sampling, and had inclusion criteria, examined. we performed adult healthy that being agreed by the chancellor and research deputy of Islamic Azad University of Hamadan in 2014, the researchers entered the

setting of the study and began to collect the data from the staff using the questionnaire by censuses method, and the checklist as instruments developed based on the purposes of the study During a visit, a medical history was taken by a physician participants were asked about doctor diagnosed high blood pressure, diabetes, high cholesterol asthma, chronic obstructive pulmonary disease and cancer.

Asthma and chronic obstructive pulmonary disease were combined into a binary variable, respiratory condition. Information was also collected on medications for hypertension, aspirin, oral contraceptive pills and hormone replacement therapy. Use of oral contraceptive pills and hormone replacement therapy were combined into a binary variable, use of sex hormones (10). The questionnaire included demographic features and the items related to the factors of obesity, and lifestyle. It was made based on the pieces of information existing in the related literature. The checklist was used to measure instances such as the extent of abdominal obesity (Waist circumference), weight, and height (measuring body mass index). To measure the waist circumstance (the area from the lowest rib to the tip) a plastic meter was used. Only the field data set, which excluded the private information such as name was uses for the study.

All participants were informed of the nature of the screening and all signed the questionnaire. The anthropometric parameters were evaluated using the respective parameters such as height, body weight, waist circumference.

According to National Institutes of Health guidelines, WC is best measured at the top of the right iliac crest using an inelastic tape measuring parallel to the floor at the end of normal expiration, (National Institutes of Health, 2000), with abdominal obesity according to the Tehran Lipid and Glucose Study after study over 30 provinces, waist circumference in the Iranian subjects-sectional, in menat least 89(cm) andwomen defined as 91(cm) will be considered (7). Body mass index (BMI) (weight/height^2 in kg/m^2) was calculated for each participant. Obesity is defined as BMI$\geq$30 kg/m^2 Blood samples were collected into the tube.

CRP measurements were performed in the laboratory. Theserum was transferred into plastic tube, and tube was stored at $-70°C$ to be used later

for hs-CRP. Plasma CRP levels were measured by means of a colorimetric competitive ELISA.

SPSS program (Version 20) was used for statistical analysis and statisticalsignificance was accepted at P<0.05. Descriptive statistics were generatedfor all variables. Data are presented as mean SD, unless stated otherwise. Spearman rank correlation coefficients were used to quantify the relations between plasma CRP levels and obesity variables.

Differences in mean values between subjects with and without obesity types were assessedusing the unpaired Student's t-test for numerical values and Chi-square test for categorical variables.

Pearson's correlation was conducted to test, using lnhs-CRP as a dependent variable and WC or BMI as independent variables stratified.

Results:

The mean age in the participants with an actual increased waist circumference was 35 (SD 8.2) years. 62.6% were male and 37.4% were female. Actual increased waist circumference was 48.4 (SD 10.7). The characteristics of the subjects are summarized in Table 1.

Table 1. Clinical profile of subjects

Number of subjects	234
Age, y	35±8.2
Waist circumference(cm)	85.1±11.4
Weight, kg	71.5±15.2
Height	167.7±8.8
BMI, kg/m2	42.4±11.11
CRP, μg/mL	3.34±5.4

Among the 260 participants, according to the CRP range, 47% of subjects in the average risk area and 15.4% were high-risk for cardiovascular diseases. The results of the data analysis showed that prevalence of overweigh was 47.5% and the relationship between overweigh and CRP was, P=0.006 (Table 2).

Waist circumference in excess of 89 cm in men was 12.7% and in women waist circumference in excess of 91 cm was 21%.

In addition, Subjects with elevated CRP had higher BMI, WC. For elevated CRP, Subjects in the highest BMI quartile had an OR of 6.27 (95%

CI, 3.69–11.9) compared with subjects in the lowest BMI quartile.

Table 2. CRP range and BMI change

BMI	CRP		
	1>	**1-3**	**≥3**
25>	0.5	0.5	1.9
25-29.9	14	28.4	7.2
30-34.9	9.2	17.9	6.8
35-35.9	3.9	6.3	2.4
40 ≥	0.5	0.5	0.0
Total	28.1	53.7	18.3
P-value=0.006			

The result shows the relationship of CRP with BMI throughout the BMI spectrum. CRP levels were strongly correlated with BMI (P=0.0002).

Levels of CRP also increased steadily across WC quartiles (P=0.0001). Waist circumference quartiles were also strongly associated with odds of elevated CRP. Women in the highest WC (91cm) and Women in the highest WC (89cm) had an odd of elevated CRP of 5.24 (95% CI, 3.15–14.0).
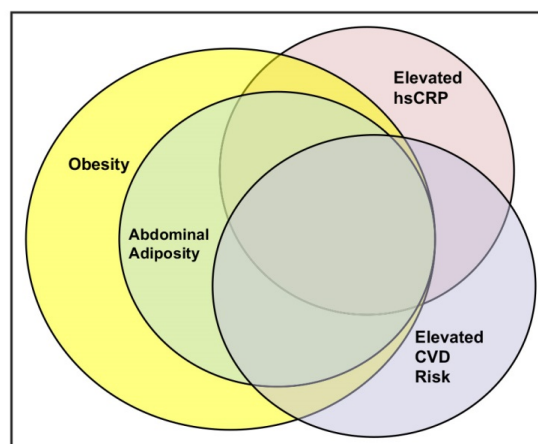

Figure1: Cardiovascular risk attributes in the overall population

Within obesity, there are those who have predominantly subcutaneous adipose tissue and those with more visceral adipose tissue who in large part make up those with abdominal obesity. Abdominal obesity is associated with elevated of hs- CRP abdominal obesity and elevated levels of hs- CRP are associated with increased risk for CVD (15)

Conclusion:

We found that CRP level was strongly correlated with BMI; inflammatory markers werealso strongly associated with waist

circumference. Risks associated withmeasures of abdominal adiposity were not independent oftotal adiposity, as measured by BMI. Among the adiposity measures that we studied, WC was the strongest predictor of elevated inflammatory markers. It is apparent from the data presented that not all obese individuals had high CRP concentrations (6). The degree of central obesity seemed to be the main determinant of an increased hs-CRP level (10).

Several studies have reported higher CRP levels among men and women with increasing BMI (11,12). The relationship between central obesity and increased levels of hs-CRP has been well studied. Adipose tissue is known to secrete cytokines that stimulate the production of hs-CRP in the liver, but adipose tissue itself may also secrete hs-CRP and thereby raise hs-CRP levels. Genetic polymorphisms could partially explain the inter-individual variability observed in the inflammatory profile of obese patients and the inter-individual variability in metabolic perturbations associated with obesity (10).

In support of this finding, report that Measures of obesity and CRP concentration were significantly associated in both ethnic groups, South Asian women and European women, Also emphasizedthat the correlation to CRP was especially strong among South Asians (P < 0.01) for measures of central obesity (13).

In all studies that choi et al (2013) analyzed, each measure of obesity was associated with CRP, regardless of age, sex and ethnicity of participants. In adults, the random-effects summary correlation coefficient between BMI and ln (CRP) was strong (Pearson coefficient [r] = 0.36; 95% CI = 0.30 to 0.42). Obesity and overweight, defined as BMI _ 30 kg m-2 and _25 kg m-2, respectively, were strongly associated with increased odds of elevated CRP. Similarly, the random-effects summary correlations between ln (CRP) with WC (r = 0.40; 95% CI = 0.31 to 0.48) and WHR (r = 0.23; 95% CI = 0.16 to 0.29) in adults were strong (14).

There is an emerging consensus that CHD has a multifactorialetiology, including atherosclerotic, prothrombotic, and inflammatory components.

Therefore, beyond the assessmentof conventional CHD risk factors, new markers have beenexplored in prospective observational studies

with the hopethat they might improve our ability to predict the risk of developing an acute coronary event (15).

In other words, cardiovascular risk stratification is used to help identify patients who will benefit from more aggressive interventions to avert future cardiovascular events. Inflammation, measured as hsCRP, has come to the forefront as a tool to better risk-stratify intermediate-risk patients. It is expected that in the new National Cholesterol Education Program Adult Treatment Panel IV guidelines, measurement of hsCRP will be considered in individuals at intermediate risk for future CVD events. Although hsCRP has value as a marker for CVD risk, this measure does little to inform clinicians of the cause of the underlying inflammatory state. Obesity is a morbid condition associated with many established cardiac risk factors, including hypertension, insulin resistance, diabetes, the metabolic syndrome, elevated lipid levels, and inflammation. Using BMI as the sole measure of obesity in multivariate models adjusted for traditional CVD risk factors has led to only modest associations with CVD risk. Measuring abdominal adiposity in addition to BMI, however, helps identify those with increased levels subclinical atherosclerosis and increased CVD risk (Figure 1) (16).

On theother hand, measuring central adiposity with WC or WHR is simple, reproducible, cost free, and available in any clinical setting. These measures can provide immediate information to cliniciansand give an unparalleled view in a simple clinical encounter of the metabolic status of a patient. In addition, increased abdominal adiposity is a reversible condition, with excellent evidence that decreasing adiposity diminishescardiovascular risk. Serial measurements of abdominalobesity may help physicians emphasize weight loss andexercise as critical lifestyle modifications to more effectivelydecrease CVD risk in their patients (16).

Moreover, Tchernof et al 2001 showed that, whether weight loss can also reduce the inflammatory state of high-risk abdominally obesity with elevated plasma CRP concentrations (17).

In the worldwide Interheart study of patients from 52 countries, nine potentially modifiable factors accounted for over 90% of the population attributable risk of a first MI. These included

smoking, dyslipidemia, hypertension, diabetes, abdominal obesity, psychosocial factors, lack of daily consumption of fruits and vegetables, regular alcohol consumption, and lack of regular physical activity (18,19)

Consequently, WHO has the unique authority and the clear mandate to lead the development and implementation of the global strategy for the prevention and control of non-communicable diseases and thereby to create a better environment for world health in 2020 and beyond (20,21)

In addition to extending understanding of the relation between adiposity and CRP concentrations, our results also provide insight into the previous observation that CRP concentrations fall when obese individuals lose weight (6). Physical activity showed a significant and inverse dose-response relationship with fibrinogen, plasma and blood viscosity, platelet count, coagulation factors VIII and IX, von Willebrand factor, fibrin D-dimer, tissue plasminogen activator antigen, C-reactive protein, and white cell count, even after adjustment for possible confounders (22,23).

Finally, hs-CRP could still be used as a prognostic marker of cardiovascular disease and diabetes. This would enable physicians to determine which centrally obese individuals should be encouraged most strongly to adapt a healthier lifestyle (10).

Our review has a number of potential limitations. First, the cross-sectional design of included studies prevents us from drawing causal inferences about the association between obesity and CRP levels. Second, anthropometric measures of obesity have limited diagnostic capacity for body fatness in adults and may result in the misclassification of patients with high CRP levels (24). However, the ease of measuring BMI, WC or WHR and the lack of reliable methods for measuring body composition leave us with BMI, WC and WHR as the predominant measures of obesity in research (25). Finally, the implementation of sex-specific CRP cut-offs might be considered for improving CVD risk assessment conducted. We further recommend that current CVD risk prediction models that are considering the incorporation of CRP to provide risk assessment methods that account for the sex-specific associations between measures of obesity and CRP.

In addition, we did not find the association between obesity and CRP to be different between male and female children. Currently, the patho-physiology leading to sex and ethnicity differences in the association between obesity and CRP in adults are not well understood. The absence of such sex difference in childhood and its emergence in adulthood could indicate a hormonal role.

Acknowledgment:

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