Evaluation of Interleukin 6 and high sensitive C-reactive protein in relation with Body Mass Index

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Abstract

Background: Obesity is one of the largest public health problem worldwide. It is a multi-factorial chronic disease that increases mortality and the prevalence of heart-related diseases. Adipose tissue secretes large numbers of peptides that resemble cytokines. Interleukin 6)IL-6(is one of those peptides that are released by adipose tissue. One of the major function of IL-6 is sending signal to liver to secrete C-reactive protein (CRP).

Objective: To study the relationship between obesity and inflammation by: estimation of high sensitive C-reactive protein (hsCRP) and IL-6 concentrations in participants sera in relation with different body mass indices (BMI).

Patients and Methods: This cross-sectional study was performed through the period of 3 months and 90 participants with the average range of age 25-40 years old were included, they were categorized into three groups (30 with BMI less than 25, 30 with BMI ranged between 25-29.9 and 30 with BMI more than 30).

Results:The concentrations mean of hsCRP was significantly elevated among the three studied groups as a result of BMI increasing (0.945 mg/L, 1.694mg/L and 2.521mg/L respectively). There was a significant increasing in the mean of IL-6 in relation with increased BMI in all included groups (1.084mg/L, 1.802mg/L and 3.531 mg/L respectively). Linear correlation between the concentrations means of hsCRP and IL-6 were found in all studied groups.

Conclusion:This study demonstrated a significant relationship between obesity and inflammatory marker (IL6 and hsCRP) .

Key words: Obesity, inflammation , hsCRP, IL-6, BMI.

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Introduction

Obesity is a chronic disease that develops from the interaction of behavioral, metabolic and psychological and molecular factors. It is caused by adipose tissue increasing and results in excessive fat accumulation Fernández-Sánchez *et al.*, 2011.

Obesity is considered the largest public health problem especially in industrialized countries (Fried et al., 1998) . Obesity increases the rate of mortality and the prevalence of diabetes, cardiovascular diseases and colon cancer (Bustard et al.,2002).

Large numbers of physiologically active peptides are secreted by adipose tissues called adipocytokines because of the related properties with cytokines. Leptin, IL-6 , tumor necrosis factor-alpha (TNF-a),

plasminogen activator inhibitor 1 , adiponectin and others are some of these adipocytokines (Alikaşifoğlu *et al.*, 2009).

IL-6 is produced by many cell types such as monocytes , fibroblasts and endothelial cells and many tissues including adipose tissue. The production of IL-6 by adipose tissue is induced in obesity (Fried et al., 1998 ; Bustard *et al.*,2002) . It is concept that 15 - 30 % of circulating IL-6 levels produces from adipose tissue in absence of acute inflammation (Mohamed-Ali *et al.*,1997).

One of the main IL-6 effects is the stimulation of hepatic CRP production which is an independent major marker of cardiovascular complications (Ridker , 2003) Also IL-6 play a central role in the association of obesity and inflammation (Yudkin *et al.*,2000). IL-6 level in adipose tissue is strongly correlated with circulating CRP and IL-6 levels (Maachi *et al.*, 2004).

Patients and Methods

A total of 90 participants were selected from Irbil city. They were all men and aged from 25-40 years old. According to BMI they were categorized into three groups. 30 participants had BMI less than (25), 30 other participants had BMI ranging between (25-29.9), and finally 30 participants above (30).

IL-6 and hsCRP were measured for all samples included in this study. Serum hsCRP levels were estimated using spectrophotometric method (Biosystems S.A., Spain) . Serum IL-6 concentrations were measured using Enzyme immunoassay ELISA kit (Beckman Coulter, France). Patients had a history of inflammation diseases and hormonal or drug therapy at the time of study were excluded .

Statistical Analysis

Spss program was used for statistical analysis and statistical difference was accepted at $p \leq 0.05$. One-way ANOVA test was used to compare between concentration means of hsCRP and IL-6 for the three groups of BMI. The correlation was analyzed with Pearson correlation coefficient to assess the relative strength of association of hsCRP and IL-6. Descriptive statistics were generated for all variables.

Results

The results of hsCRP concentrations for the three groups showed that there are a significant differences ($p \leq 0.05$) among groups according to BMI. Table (1) Shows the result of statistical analysis for hsCRP of three groups of BMI, where hsCRP concentration raised as a result of BMI increasing . Also figure (1) shows the relationship between hsCRP and BMI.

Table (1): hsCRP level of participants serum.

Groups	Number	Range mg/L	Mean mg/L	SD	SE
BMI<25	30	0.22-2.7	0.945	0.692	0.089
BMI=25-29.9	30	0.77-3.2	1.694	0.555	0.071
BMI≥30	30	1.77-3.4	2.521	0.432	0.064

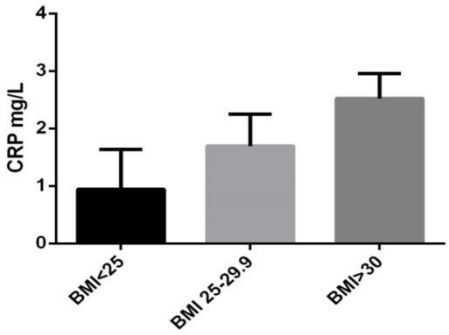
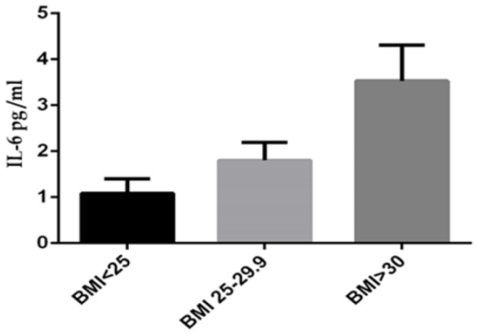


Figure (1): The relationship between hsCRP concentrations and BMI

Data analysis of IL-6 concentrations result revealed that means of IL-6 in the three groups of BMI were significantly different ($p \leq 0.05$). IL-6 level in third group was higher than second group of BMI and second group was higher than first group of BMI , table (2) . Figure (2) shows the relationship between IL-6 and BMI.

Table (2): IL-6 level of participants serum.

Groups	Number	Range pg/ml	Mean pg/ml	SD	SE
BMI<25	30	0.62-2.06	1.084	0.316	0.040
BMI = 25-29.9	30	1.07-2.57	1.802	0.387	0.050
BMI ≥30	30	2.00-4.99	3.531	0.775	0.100



Figure(2): The relationship between IL-6 concentration and BMI.

Levels of hsCRP were positively correlated with IL-6 levels according to the correlation coefficient (r=0.677, p=0.000), figure (3).

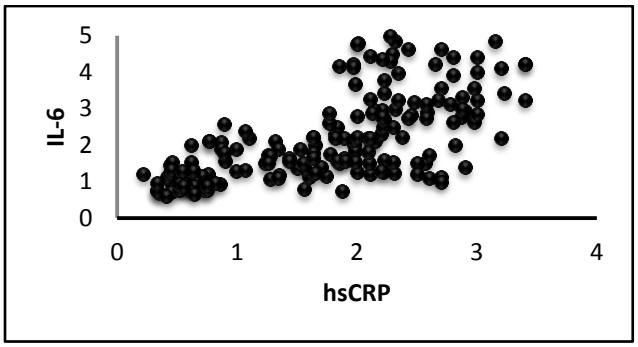


Figure (3): Correlation between serum level of hsCRP and IL-6 in participants sera.

Discussion

Immunity and metabolism are two main systems for survival and are closely associated with each other. Obesity are linked with immune activation and caused inflammation while malnutrition lead to immunosuppression (Wellen and Hotamisligil 2005) , from this theory the present study was designed to examine the relationship between obesity and inflammation. Two of high sensitive inflammatory markers were chosen to analyzed collected sera samples which were hsCRP and IL-6, samples were categorized into three groups according to the BMI.

Excess body fat is linked to increased mortality and morbidity by effecting the development of diseases as diabetes type II and cardiovascular disease . Chronic inflammation in adipose tissue may be a mediator of diseases associated with obesity. Pro-inflammatory cytokines influence adipose tissue function and could cause metabolic disorders. Also circulating cytokines concentrations may be increased in obesity (Alvehus,2012). Over the world, more than 1 billion adults are overweight, 300 million of whom are having a BMI equal to or greater than 30 kg m–2 (WHO,2002).

In this study ,hsCRP levels were found to be elevated according to increase grade of obesity where the mean of hsCRP in group of BMI>30 recoded highest value (2.521 mg/L) among means of other BMI groups. This elevation gave significant differences $p \leq 0.05$.Khan *et al.* (2011)comparison agreed with present study which showed significant difference in CRP and TNF-α levels between individuals with normal weight (BMI<30) and obese individuals (BMI>30) . Choi *et al,(*2013) concluded that obesity is associated with elevated levels of CRP, also they referred to there was no any association between CRP levels and obesityin male and female children. Dandona et al. (1998) result corresponded with present work they found inflammatory markers such as CRP and TNF-α levels were elevated in obese individuals. Fat cells numbers are completed during childhood and adolescence and remains constant during adulthood in lean and obese individuals. fat mass enlargement

is due to hypertrophy in adults while weight loss is linked to decrease adipocyte volume (Spalding *et al.,* 2008). This is important because hypertrophic adipocytes are responsible of expression and secretion some cytokines and adipokines (Skurk *et al.,* 2007).

Regarding the results of IL-6 , it levels were elevated as a result of BMI increasing where the BMI≥30 recorded highest value among other groups. Obese adipocytes are important source of inflammatory cytokines and chemokines such as IL-6, TNF-alpha, monocyte chemoattractant protein-1 and dysregulated production of adiponectin which anti-inflammatory adipokines (Guilherme *et al.,* 2008). IL-6 is a multifunctional cytokine produced by several immune cells and non-immune tissues. IL-6 stimulates the liver to produce of acute-phase proteins such as CRP, which increase 1000fold in acute inflammation and slightly elevated during low grade inflammation (de Ferranti and Mozaffarian ,2008). IL-6 able to modulate immune response, interfere with lipid and glucose metabolism and impairs adipocyte differentiation (Gustafson, 2010). Adipose tissue is an important source of IL-6 therefore the production of IL-6 increases with fat mass, fat is responsible of 30% of systemic IL-6 levels, approximately (Mohamed-Ali *et al.,* 1997). Another source of IL-6 is skeletal muscle (Pedersen and Febbraio, 2008).

Study of Bastard et al. (2000) and Kern et al., (2001) agreed with present study, they found positive correlation of IL-6 level with BMI, especially in obese individuals. The exposure of adipose tissue to IL-6 lead to increase lipolysis due to the IL-6 influences on lipid metabolism, (Trujillo *et al*., 2004). This study referred to positive correlation of CRP and IL-6 levels elevation (r= 0.677). Dandona *et al.* (1998) and Maachi et al., (2004) study resembled with present result , they showed there is a positive association between the levels of IL-6 in adipose tissue and CRP levels in obese individuals. Chemokines have important role in the inflammation process and macrophages recruiting to adipose tissue. (Weisberg *et al.,* 2003).

Macrophages numbers are positively correlated with body mass and adipocyte size. Accumulated macrophages are considered to be responsible of adipose tissue inflammation since they are the main source of pro- inflammatory cytokine production (IL-6 and TNF-alpha) in adipose tissue (Cancello *et al*., 2005). After weight loss , macrophage infiltration and expression of pro-inflammatory cytokines in adipose tissues are reduced (Po-Shiuan Hsieh ,2011; Bruun *et al.,* 2006; Cancello *et al*., 2005). CD8 T cells play the important role in recruitment of macrophage into adipose tissue. Large numbers of CD8 T cells infiltrated into adipose tissue and induced the macrophages accumulation mice. (Nishimura *et al.,* 2009).

Conclusion

1-There is a proportional relationship between BMI and CRP in men.

2-There is a proportional relationship between BMI and IL-6 in men.
3-Linear correlation was obtained between hsCRP and IL-6.
4-Obesity induce inflammation in adipose tissues.

Recommendation

1-Measure the level of serum IL-6 and hsCRP in the athletics.
2-Determine the relationship linked the CRP and BMI with obesity in women.
3-Study the ability of obesity therapy by immune response modulation.
4-Study the relationship between CD8 T cells and obesity.
5-Comparison study of serum IL-6 and hsCRP levels between male and female groups according to BMI.

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