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Association between Serum Monocyte Chemoattractant Protein 1 Concentration and Lipid Parameters in Obese Women.

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ABSTRACT

Obesity induces systemic inflammation implicating in the development of many of its clinical complications. Monocyte chemoattractant protein-1 (MCP-1/CCL2) is a chemokine implicated in the pathogenesis of hypercholesterolemia. this study aims to estimate serum MCP-1/CCL2 and CRP in obese women without metabolic complications as comparing to normal non obese women and to evaluate the association between MCP-1/CCL2 and lipid parameters in obese women. This cross-sectional study was conducted on 90 obese women aged 25-35 years and 90 age matched non-obese healthy women as controls. Anthropological study included weight and height measurement for all the subjects, also fat mass, fat-free mass and body fat percentage measures. Laboratory tests included blood glucose, ALT, AST, cholesterol, HDL, LDL, triglycerides and albumin. CRP and MCP/1 serum levels were estimated. Serum triglycerides, LDL, CRP and MCP-1/CCL2 were significantly higher in obese women than non-obese. Serum MCP-1/CCl2 was significantly correlated with serum cholesterol, triglycerides and LDL in obese women. Serum CRP was significantly correlated with body mass index and fat mass. High levels of serum MCP-1/CCL2 concentration were independently associated with elevated lipid parameters and may contribute to the development of hypercholesterolemia in obese women.
Keywords: Obese women, CCL2, CRP, adipose tissue, monocyte, inflammation, chemokine.

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INTRODUCTION

Obesity is a common condition increasing in prevalence worldwide [1] and becomes one of the most important public health problems [2]. At least 1.1 billion adults are overweight including 312 millions who are obese [3,4].

Obesity is a high risk factor for the development of many metabolic and cardiovascular complications. [5]. The common feature of these complications is a low-grade inflammation characterized by elevated circulating levels of pro-inflammatory cytokines and chemokines as well as accumulation of immune cells (macrophages, lymphocytes) in the adipose tissue [6].

Adipose tissue-derived chemokines are significant factors in driving adipose tissue macrophages recruitment during obesity [7] and involved in the pathogenesis of atherosclerosis [8,9].

Accenting the role of inflammation in obesity, adipose tissue from obese human beings is characterized by inflammation and can secrete humoral factors that regulate systemic acute-phase reactants, such as C-reactive protein (CRP) [10,11] as well as inflammatory factors, as monocyte chemoattractant protein 1 (MCP-1), also known as CC chemokine ligand 2 (CCL2) [12,13].

Chemokines constitute a family of chemoattractant cytokines, monocyte chemoattractant protein-1 (MCP-1/CCL2) is one of the key chemokines that regulate the migration and infiltration of monocytes/macrophages. [14] Human MCP-1/CCL2 is composed of 76 amino acids and is 13 kDa in size [15] and its expression is highest in the stromal vascular fraction of white adipose tissue, where macrophages are abundant [16].

Hyperlipidemia is characterized by increased serum level of lipids and lipoproteins and is a risk factor for atherosclerosis. Inflammation plays a crucial role in the formation and progression of atherosclerosis and accordingly on cardiovascular diseases. [17] In experimental and clinical studies, several inflammatory markers such as C-reactive protein are associated with lipids level dysregulation [18].

The aim of this study is to estimate MCP-1/CCL2 and CRP in obese women without metabolic complications as compared to normal non-obese women and to evaluate the association between MCP-1/CCL2 and lipid parameters in obese women.

SUBJECTS AND METHODS

This cross-sectional comparison study of obese and non-obese subjects was conducted on 180 women attending National Research Centre (NRC) Obesity Clinic. Their age ranged from 25 to 35 years old.

All the procedures used in this study were in accordance with the guidelines of the Helsinki Declaration on Human Experimentations. The study was approved by local ethics committee of the National Research Centre (No: 13176); the purpose of the protocol was explained to both the patients and control women, and written informed consent was obtained from them before beginning the study.

They were categorized according to body mass index (BMI) into Group I 90 obese (BMI from 30 to 40) and Group II 90 non-obese women (BMI 20 to 25) within the same age range as control group. All women included in this study were non diabetics, non-smokers and without signs of metabolic syndrome. [19] They were not taking any medication known to interfere with the immune function or lipid/glucose metabolism and were weight stable for more than three months.

All subjects were subjected to full clinical examination and history taking. Systolic and diastolic blood pressures (SBP, DBP) were measured using a sphygmomanometer. Weight and height were measured for all the subjects. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters (kg/m^2),

The height was measured to the nearest 0.1 cm using a fixed stadiometer (Seca), and the weight was determined to the nearest 0.01 kg using a Seca Scale Balance, with the subject wearing minimal clothing and no shoes. Waist and hip circumferences were measured and waist to hip ratio was calculated.

Body composition was measured using bioelectrical impedance analysis (BIA) with TANITA SC- 330. The same investigators performed all the anthropometric to minimize inter investigators variability. Bioelectrical impedance analysis (BIA) measures the fat mass and fat-free mass, body fat % indicating percentage of fat in human body.

After overnight fasting, 4ml venous blood was withdrawn under sterile conditions then centrifuged and serum was separated and stored at -20^{o}C.

Laboratory investigations included fasting blood glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholesterol, high density lipoprotein (HDL), triglycerides and albumin using Hitachi autoanalizer. Low density lipoprotein (LDL) was calculated. Circulating levels of CRP and MCP-1/CCL2 were estimated using commercial available R&D systems kit by enzyme linked immunosorbent assay (ELISA), assays were performed according to manufacturer's instructions. [16]

Statistical Analysis: Data were collected and analyzed using Statistical Package for Social Science version 13 (SPSS Inc., Chicago, IL, USA). Independent t-test was used in the comparison between two groups with quantitative and parametric distribution. Pearson correlation was used to assess the significant relation between two quantitative parameters.

RESULTS

Group I Obese women were diagnosed as BMI ranging from 30 to 40 kg/m^2 while Group II included normal weight women with BMI range 20-25 kg/m^2.

Significant increase were shown in BMI, waist and hip circumferences, waist/hip ratio, fat mass and body fat % in obese women (Group I) as compared to normal women (Group II) Table 1.

Triglycerides, LDL, CRP and MCP-1/CCL2 were significantly increased in obese women (Group I) than normal women (Group II) as shown in Table 2.

CCl2 was positively significant correlated to serum cholesterol, triglycerides and LDL as shown in Table 3.
CRP was positively significant correlated to BMI and fat mass as shown in Table 4.

Table 1 Clinical and anthropometric measures

parameter	Group I (N=90) Obese	Group II (N=90) Controls	p-value
BMI (Kg/m^2)	38.34±3.18	22.207 ± 4.12	0.05
SBP (mmHg)	118.6±17.39	108.33±18.95	0.802
DBP (mmHg)	75.42±11.84	70.33±12.73	0.809
Waist circumference (cm)	106.42±10.00	99.46 ±10.39	0.001
Hip circumference (cm)	125.22 ± 10.81	112.01±10.91	0.001
WHR	0.86 ± 0.05	0.82 ±0.13	0.001
Fat mass (Kg)	44.19±13.91	18.89±8.51	0.046
Body fat %	44.83±7.16	28.97±9.55	0.006

Data are presented as mean ±SD, P≤0.05 is statistically significant

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Table 2 Laboratory tests done for both groups

parameter	Group I (N=90)	Group II (N=90)	p-value
Blood glucose (mg/dl)	97.15±47.53	99.67±76.26	0.47
ALT (IU/L)	20.95±17.16	20.19±15.73	0.89
AST (IU/L)	23.22±9.49	22.29±9.06	0.76
Cholestrol (mg/dl)	193.15±47.13	196.45±53.62	0.31
Triglycerides (mg/dl)	135.43± 23.89	95.45±24.84	0.002
HDL (mg/dl)	46.73±14.41	49.27±15.49	0.677
LDL (mg/dl)	134.84±17.89	97.23±22.54	0.01
Albumin (gm/dl)	4.478±0.42	4.595±0.34	0.426
CRP (mg/dl)	10.84±23.26	2.68±4.26	0.001
CCL2 (pg/ml)	75.852±66.92	37.504±34.07	0.001

Data are presented as mean ±SD, P≤0.05 is statistically significant

Table 3 Pearson correlation between MCP-1/CCL2 and cholesterol, triglycerides and LDL in obese women (N=90)

parameter	r	p
Cholesterol	0.359	0.003
Triglycerides	0.276	0.025
LDL	0.356	0.004

r=correlation coefficient, p≤0.05 is statistically significant

Table 4 Pearson correlation between CRP and BMI, fat mass in obese women (N=90)

parameter	r	p
BMI	0.294	0.005
Fat mass	0.267	0.012

r=correlation coefficient, p≤0.05 is statistically significant

DISCUSSION

The monocyte chemoattractant protein-1 (MCP-1/CCL2) is a member of the C-C chemokine family and is a potent chemotactic factor for monocytes. In obesity, upregulation of MCP-1/CCL2 is associated with macrophage accumulation and activation in adipose tissues as well as insulin resistance. [16] Many studies identified the role of MCP-1/CCL2 in the pathogenesis of initiation and progression of atherosclerosis. MCP-1/ CCL2 is highly expressed in atherosclerotic lesions and its role in atherogenesis is reliable. [20] In humans, elevated MCP-1/CCL2 serum levels were detected in patients with diabetes mellitus and in subjects with risk factors for atherosclerosis as hypertension, renal failure, hypercholesterolemia, vascular diseases and coronary artery disease. The genetic variation in the MCP-1/CCL2 gene is associated with elevated serum concentration of the chemokine and higher prevalence of myocardial infarction. [21]

The role of inflammation in the initiation and progression of cardiovascular diseases is well recognized. Systemic inflammation and immune system play a vital role in the atherogenesis. The atherosclerosis process depends on the state of continuous low-grade inflammation and the presence of lipid abnormalities revealing the association between hyperlipidemia and inflammatory status. [18]

Our results revealed significantly higher serum triglycerides and LDL in obese women (Group I) as compared to control (Group II) this is in agreement with Chang et al. [13]

Our results revealed significantly higher serum MCP-1/CCL2, and CRP values in obese as compared to normal women this was in agreement to Utsal et al [22], Breslin et al [23] and Chang et al [13] indicating a pro inflammatory condition. Taube et al [24] stated that adipocytes of obese subjects are characterized by increased release of MCP-1.

Serum CRP was positively significant correlated to BMI (r= 0.294,p= 0.005) this is in accordance with Chang et al [13] and DaCosta et al [10] who stated that adipose tissue secretes many cytokines, such as the proinflammatory tumor necrosis factor alpha and interleukin 6, which trigger the hepatic production of acute

phase proteins as CRP. Bahceci et al [25] showed that CRP is positively correlated with adipocite size. In this study CRP was positively significant correlated to fat mass (r=0.267, p=0.012) this is in agreement with Lemieux et al [26]. Tsuriya et al [27] stated that visceral fat mass was a significant and independent predictor for serum CRP levels.

Our results showed significant correlation of MCP-1/CCl2 to cholesterol, triglycerides and LDL (r=0.359, p=0.003; r=0.276, p=0.025; r=0.356, p=0.004 respectively) this is in agreement with Lim et al [16]. Also, Garlichs et al [28] found increased serum level of MCP-1/CCL2 with hypercholesterolemia.

No correlation between serum MCP-1/CCL2 and CRP was detected in this study and this is similar to Piemonti et al [29] results.

In conclusion high serum level of CRP and MCP-1/CCL2 detected in obese women as compared to controls is indicating an inflammatory response condition. Also, high level of serum MCP-1/CCL2 concentration is independently associated with elevated lipid parameters; cholesterol, triglycerides and LDL.

Conflict of Interest

Authors have no conflict of interest to declare

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