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Adiponectin Level In Relation To Lipid Profile, Inflammatory Markers, Insulin Resistance and Sex Hormone Binding Protein in Obese Adults.

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ABSTRACT

Obesity and metabolic syndrome are considered to be chronic inflammatory states in which macrophages accumulate in adipose tissue and secrete inflammatory cytokines. The aim of this study was to investigate the relationship between inflammatory markers (hs-CRP), adiponectin, and the components of MS(dyslipidemia,insulin resistance and hypertension) as well as sex hormone binding protein in a group of Egyptians suffering of obesity . All patients and controls underwent clinical measurements of height, body weight and body mass index(BMI).Laboratory investigations included lipid profile, fasting blood glucose ,insulin ,insulin resistance(IR),high sensitive c-reactive protein ,and sex hormone binding globulin . Adiponectin level was low among the obese group when compared to the control group. Correlation analysis in both groups revealed that adiponectin and sex hormone binding globulin inversely related to BMI ,age, systolic blood pressure ,diastolic blood pressure ,fasting blood glucose, cholesterol ,triglycerides ,IR and hs-CRP .In conclusion These findings are of clinical significance in terms of screening based on metabolic health phenotype to identify those at greatest cardiometabolic risk and progression of the disease, for whom appropriate therapeutic or intervention strategies should be developed . Such tests may have utility in motivating physicians and patients' families toward lifestyle changes, ultimately improving prevention efforts

Keywords: Adiponectin, Lipid Profile, Sex hormone, obesity

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INTRODUCTION

Adiponectin (APN), a 30 kDa adipocytokine, is constitutively present in high concentrations in human plasma as a low molecular weight (LMW), a middle molecular weight (MMW), and a high molecular weight (HMW) form. Adiponectin is mainly produced by adipose tissue but cardiomyocytes are also capable of synthesizing APN and express its receptors, APN receptor 1 (APN-R1) and APN receptor 2 (APN-R2). 1,2 Adiponectin exhibits immune modulator, anti-proliferative, anti-apoptotic, and pro-angiogenic effects and APN plasma concentrations are inversely correlated with classical cardiovascular risk factors such as body mass index (BMI), hypertension, and diabetes(3). Emerging data suggest that adiponectin is the link between obesity and obesity-related disorders with cardiovascular disease. Adiponectin is a dominant insulin-sensitive adipokine and, in contrast to other adipose-tissue derived cytokines, it has major anti-diabetic, antiatherogenic and anti-inflammatory properties [1-4].

Abnormal fat accumulation is associated with inflammatory changes, including recruitment of macrophages and activation of endothelial cells, which promote vascular disease [5]. Adiponectin correlated with endothelial – dependent vasodilatation and was found to have potent anti- inflammatory effects on the cellular component of blood vessel walls [6].

In obese patients, a low-grade systemic inflammation has been reported [7], as shown by increased CRP and IL-6 levels compared to those observed in lean subjects. Macrophages from adipose tissue have been shown to contribute to up to 30% of circulating IL-6,indicating that adipose tissue is a significant production site of circulating pro inflammatory cytokines . Adiponectin has been shown to be involved in insulin sensitivity. The influence of adipokines on immunity and inflammation has been well documented. In most inflammatory diseases, it is generally accepted that leptin displays pro inflammatory effects, while adiponectin is considered to primarily act as an anti-inflammatory molecule ,that is potentially antiatherogenic [8]. SHBG is a carrier protein produced by the liver. Its main function is to transport sex steroids, but it has potential insulin sensitizing effects independent of its transport function [9]. Recently, the ability of SHBG to predict development of diabetes has been reported in both men and women, generating new interest in this protein as a marker for the development of metabolic disease [10]. Sex hormones are known to change over the menopausal transition, whereas SHBG remains relatively constant [11].

The aim of this study was to investigate the relationship between inflammatory markers (hs-CRP), adiponectin, and the components of MS(dyslipidemia,insulin resistance and hypertension) as well as sex hormone binding protein in a group of Egyptians suffering of obesity .

METHODS

Eighty six obese patients and 26 non obese adults were included in this study. Informed consents were obtained from patients of our study group according to the guidelines of the ethical committee of the National Research Centre. Obese and non-obese were recruited from the outpatient clinic of National Research Centre during the period between 2009-2010. Obese patients had BMI greater than or equal to 25 whereas non obese had BMI below 25.
Patients who had secondary obesity such Cushing syndrome ,with corticosteroid therapy etc. were excluded.

All the patients in the study were subjected to the following : a full history taking including complete present history ,family history and past history ,clinical examination ,both general and systemic with particular emphasis on weight (wt),height(Ht) and BMI (calculated by dividing the patient weight in Kg by the square of the height in mitre Kg/m2,

Laboratory investigations

Blood samples; five ml. of blood were withdrawn from the anticubital vein, after fasting for 14 hours under aseptic conditions. Serum was collected to evaluate the following parameters:

- Lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglyceride) by using Olympus AU400 autoanalyzer.
- Insulin by chemiluminescence using Immulite.

- Adiponectin by ELISA kit (Ray Biotech,Inc)
- High sensitive C-reactive protein (Immulite)
- Sex hormone binding globuline by ELISA kit.

Statistical analysis

Data are reported as the median±SD.Data for control subjects and patients with obesity were compared using the Mann-Whitney test. Correlations were determined by Spearman's rank correlation. The results were considered to be significant when $P < 0.05$. A statistical analysis program (All statistical calculations were carried out using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows.

RESULTS

This study included 112 adults,among them 26 were normal weight(12 males and14 females) and 86 were obese.

Table 1: Clinical characteristics of study groups

Parameter	Cases(N=86)	Control group(N=26)
Age	40.13±12.9	25.4±7.8
BMIi(wt./Ht2)	37.05±.4	21±0.8
SBP mmHg	121.6±5.9	108±6
DBP mmHg	78.8±9.3	71.1±3.3

The obese group ranged in age from 20-57 years,mean age40.13 ±12.9 .Our study showed a statistically significant elevation of both systolic and diastolic blood pressure in the obese patients group than in the control group($p<0.005$ and <0.001 respectively.

Table 2: Laboratory characteristics of the study group

Parameter	Cases(N=86)	Control(N=26)	P value
FBS mg/dl	1o5±10.02	85±14.67	0.001
Chol. mg/dl	219±46.6	176. ±2.64	0.001
Tg.mg/dl	122.6±62.8	75±31.4	0.002
HDL mg/dl	45.3±11.5	42.9±11.5	0.011
LDL mg/dl	149.1±42	118.9±28	0.011
Insulin IU/ml	9.6±4.5	5.1±1.4	0.001
Insulin resistance	2.5±2.7	1.18±0.88	0.011

There is statistically significant elevation of both TG and cholesterol in the obese group in comparison to the control group. In terms of LDL and HDL, the mean value were found to be higher in obese group than in the control group.

Table 3: Inflammatory markers and sex hormone binding globulin.

Parameter	Cases(N=86)	Control (N=26)	Pvalue
Adiponectin ug/ml	10.04±14.53	45.13± 4.7	0.001
hsCRP mg/dl	12.6±18	1.5±1.4	0.022
SHBG	3o.9±2.5	60.1±15.3	0.001

The mean serum Adiponectin level in the obese group was (10.04±14.53ug/ml),which was lower than that in the control group($p<0.oo1$) ,in which the mean serum adiponectin level was 45.13±4.7. The mean serum level of Sex hormone binding globulin in the obese group was 3o.9±12.5,which was lower than that in the control group .The mean level of the High sensitive C-reactive protein in the obese group was 12.6±18mg/dl ,which was significantly higher than that in the control group . .

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Table 4: Correlation between Adiponectin and different variables

	R	P
Age	0.051	0.027
BMI	0.2	-0.165
Chol.	0.47	0.008
Tg.	0.18	0.040
HDL	-0.64	-0.162
hs CRP	-0.23	0.04
IR	-0.28	-0.051
SHBG	-0.15	-0.001

BMI body mass index,hsCRP high sensitive C reactive protein,IR insulin resistance,sex hormones binding globulin.$p<0.05$ or $p<0.001$ were considered significant.

As regards correlations, high sensitive C-reactive protein were positively correlated with BMI, LDL, Cholesterol and TG. Aiponectin and serum Sex hormone binding globulin level was negatively correlated with BMI, LDL, Cholesterol and TG.

DISCUSSION

Obesity and metabolic syndrome are considered to be chronic inflammatory states in which macrophages accumulate in adipose tissue and secrete inflammatory cytokines **,** lower adiponectin level, these factors, indicative of chronic systemic low-grade inflammation, are believed to be involved in the pathogenesis of cardio vascular disease, insulin resistance and type 2 diabetics [5].

This study examined the relation of adiponectin levels to metabolic risk factors for cardiovascular disease, including markers of atherogenic dyslipidemia (levels of plasma TG,HDL-chol.)and insulin resistance, sex hormone binding globulin(SHBG), as well as inflammatory markers (hsCRP).

The study revealed low adiponectin level and elevation of high sensitive C-reactive protein among the obese group in comparison with the control group . These results were in agreement with Tam et al 2012 [5] who reported serum markers of inflammation (Leptin, high sensitive C-reactive protein (h-SCRP) interleukin-6, tumor necrosis factor alpha , were increased among the obese patients and showed that h-SCRP levels particularly decreased after dietary control and weight loss. This study also addressed the relationship between inflammatory markers (Adiponectin, hsCRP) and metabolic syndrome criteria. This is in agreement with Chu et al 2012 [12]who reported that patients with low Adiponectin levels were at significantly increased risk of dyslipidemia and Mets. Ezzat et al 2012 in addition detected fatty liver which was inversely related to adiponectin serum levels, but this relation did not reach the significant value in adults. The most widely accepted and successful treatment for fatty liver is dietary and lifestyle changes aimed at reducing body weight. Inflammatory status is positively associated with metabolic syndrome in obese individuals.

The study also showed that adiponectin plasma levels were inversely related to triglyceride levels, fasting insulin levels these results are in agreement with Mussad & Haures 2007 [6] who also reported that adiponectin correlated with endothelial-dependent vasodilatation and was found to have potent anti inflammatory effects on the cellular components of blood vessel walls. Potential mechanisms for the protective role of adiponectin on endothelial cells include expression of cell adhesion molecules and inducing inhibitors of metalloproteinases via interleukin (IL) [10]. They also reported that adiponectin is both a marker and possibly a mediator of CVD, as it has a good potential to cardiovascular events. The study also showed a significant decrease of sex hormone binding globulin level in the obese group when compared to the control group,these results were in agreement with results of Janssen et.al,2010 which have also indicated an important relationship between sex hormone binding globulin (SHBG) and MS components . In these reports, SHBG had a stronger relationship with obesity and metabolic disease endpoints than did estrogen or testosterone [13, 14]. As regards insulin sensitivity our study showed a significant correlation to the metabolic syndrome in the obese group of patients this is in agreement with Shaibi et al 2007 who reported that correlation among the overweight & Latino youth. Therefore it is plausible that interventions targeting

improvements in these parameters may lead to reductions in overall chronic diseases such as diabetes and cardiovascular disease.

These findings are of clinical significance in terms of screening based on metabolic health phenotype to identify those at greatest cardiometabolic risk for whom appropriate therapeutic or intervention strategies should be developed. In conclusion Future efforts continue to be needed to identify clinical and laboratory characteristics that could be used as screening tests to predict disease progression. Such tests may have utility in motivating physicians and patients' families toward lifestyle changes, ultimately improving prevention efforts

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