International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
DOI: 10.22192/ijarbs Coden: IJARQG(USA) Volume 5, Issue 2 - 2018

Research Article

DOI: http://dx.doi.org/10.22192/ijarbs.2018.05.02.009

Study of the Plasma levels of Leptin and inflammatory cytokines in Egyptians with metabolic syndrome

Arafat Kassem[1], Mohamed Rashed[2]
[1]Department of Internal Medicine, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[2]Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
*Corresponding author: *Arafatkassem1970@yahoo.com*

Abstract

This study was designed to determine the plasma levels of Leptin,C-reactive protein (CRP), interleukin 6 (IL-6), and tumor necrotic factor alpha (TNF-α) in Egyptian subjects with metabolic syndrome and to examine the relationship between the criteria of metabolic syndrome with both CRP and Leptin. **Subjects and Methods:** This study made up of one hundred adults with metabolic syndrome, and fifty age and sex matched subjects without metabolic syndrome. Metabolic syndrome was explained based on the National Cholesterol Education Programme-Adult Treatment Panel III criteria. Written informed consent was acquired from the candidates. Full medical history, and physical examinations including blood pressure assessment were done and venous blood samples were drawn after an overnight fast. **Results:** There were no significant difference between subjects with and without metabolic syndrome as regard age and sex. However they differed in some demographic and clinical parameters such as smoking history, body mass index, waist/hip ratio,waist circumference, systolic blood pressure, and diastolic blood pressure, for all the *P* value was 0.001.There were statistically significant difference between subjects with and without metabolic syndrome in some laboratory variables in the form of high density lipoprotein (HDL) ($P = 0.008$), and insulin resistance (IR) ($P = 0.001$). Also, there was a statistically significant elevation in Leptin ($P=0.001$), CRP ($P = 0.003$), and the cytokines in the form of IL6 ($P = 0.001$) and TNF-α ($P = 0.001$)between the subjects with and without metabolic syndrome. There was also a significant correlation between CRP with IR, HDL-C, LDL-C, Triglyceride, IL-6, TNF-α, and Leptin in our subjects with metabolic syndrome ($P < 0.05$). Finally, there was a significant correlation between Leptin with all variables of metabolic syndrome ($P< 0.05$) except triglyceride and LDL-C levels. **Conclusion:** Plasma levels of Leptin and inflammatory cytokines are raised in subjects with metabolic syndrome and this may allocate new policies for management of metabolic syndrome and its related sequlae.

Keywords: Metabolic syndrome, Leptin, Inflammation, Insulin resistance, and Obesity

Introduction

The metabolic syndrome has been defined as a group dangerous risk factors for cardiovascular disease and type 2 diabetes, which comprises of abdominal obesity, hyperlipidemia, hypertension, diabetes (if not yet present) and raised fasting plasma glucose (1, 2). It is a manifold risk factor that emerges from insulin resistance accompanying abnormal adipose tissue (1). Clinical manifestations of metabolic syndrome may include: hypertension, diabetes mellitus,abdominal obesity, hypertriglyceridemia, lowered high density lipoprotein cholesterol. According to International Diabetes Federation (IDF) the metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions: obesity – waist circumference ≥94 cm in men and ≥80 cm in women; blood pressure≥ 130/85 mmHg (or receiving drug therapy

for hypertension); fasting glucose ≥100 mg/dl (or undergoing therapy); triglyceride ≥150 mg/dl (or receiving treatment); HDL – C<40 mg/dl in men and<50 mg/dl in women (or receiving drug therapy) (2,3).Extensivedata suggests that patients achieving these diagnostic criteria have an increased risk for significant clinical outcomes: twofold risk of coronary artery disease, increased risk of stroke, non-alcoholic fatty liver disease, diabetes and cancer (4). The parameters of the syndrome are risk factors for atherosclerosis, making metabolic syndrome an important risk for coronary heart disease(5).Obesity and IR also provide significant risk for developing type 2 diabetes(6).

Leptin, a cytokine-like molecule secreted by adipose tissue, modulates adipose tissue mass and body weight by impeding food intake and stimulating energy expenditure. Leptin increment obesity, type 2 diabetes mellitus, hypertension and metabolic syndrome. Various studies suggesting that Leptin may serve as a biomarker for obesity, insulin resistance and metabolic syndrome(7, 8). Role of Leptin as a biomarker for metabolic syndrome has been studied in different populations. Regardless of which demographic features studied, an elevated Leptin levels are associated with metabolic syndrome. This is not amazing given that elevated Leptin is associated with insulin resistance, obesity, myocardial infarction, and congestive heart failure (9).

Current theories on the pathophysiology of the metabolic syndrome have it that inflammation is the connection between abdominal obesity, insulin resistance and cardiovascular disease in the metabolic syndrome(10). Interleukin 6 (IL-6) and Tumor necrosis factor alpha (TNF-α) are proinflammatory cytokines that have been associated with abdominal obesity and the metabolic syndrome (11, 12, 13, 14 and 15). IL-6 has been associated with increased secretion of C-reactive protein in the liver, atherosclerosis, and cardiovascular mortality (15). Current theories of insulin as an anti-inflammatory hormone have been reported(10, 11), and disability of insulin action in insulin resistanceevoked by the proinflammatory state of excess fat tissue mass would explain the association between abdominal obesity, insulin resistance, and the metabolic syndrome (10).This study was outlined to measure the plasma levels of Leptin, IL-6, TNF-α, and CRP in Egyptiansubjects with metabolic syndrome and to determine the link between variables of metabolic syndrome withLeptin and C-reactive protein in Egyptian subjects. The outcome of inflammation in metabolic syndrome may improve our knowledge to develop new concepts for the management of metabolic syndrome and related sequelae.

Subjects and Methods

This prospective case–control study consisted of one hundred adult subjects with metabolic syndrome and fifty age and sex matched controls without metabolic syndrome in the period between April 2016 to March 2017. The diagnosis of the metabolic syndrome was based on WHO, NCEP-ATPIII, and IDF criteria (3). The subjects with metabolic syndrome were recruited from Outpatient Clinics of the Internal Medicine Department of El-Hussein University Hospital and the controls were normal persons from staff of the hospital. The Ethical Research and Review Committee of the Hospital approved the study protocol, and informed consent was obtained from all participants.

The inclusion criterion was an adult male or female between 40 and 55 years. Patients with hypertension, diabetes mellitus, ischemic heart disease, chronic renal disease, cerebrovascular stroke, peripheral vascular disease, and chronic liver disease were excluded from this study.

Abdominal obesity was determined by measurement of the waist circumference in centimeters using the pubic crests and the lower border of the ribs as landmarks. The hip circumference was measured from the outermost point on the gluteus muscle using the neck of the femur as an anatomical indicator.

Measurement blood pressure was done using the Mercury Sphygmomanometer (cuff size 15 cm × 42 cm). The subjects were rested on his/her back for about 30 min. before measurement. The systolic blood pressure was cited as the first korotkoff sound and diastolic one as the fifth korotkoff sound. The last two measurements were averaged for analysis.

Total Cholesterol (TC), high density lipoprotein (HDL cholesterol) and serum triglycerides (TG)were measured by enzymatic method using commercial kit provided from Roche Diagnostics, and LDL was calculated by the equation (LDL=cholesterol - triglycerides/5 –HDL).Fasting blood glucose was determined using the enzyme based Glucose hexokinase kit. Glycated hamoglobin A1C was measured using a column chromatography method by

commercial kit provided from Biosystem Company, Barcelona, Spain. After final rinse washing the result was determined photometrically using photometer (Reference range 5.1-6.4%). Insulin level: was estimated using a commercially insulin kit (Immunotech, Marseille, France) which was modified for use in microtiter plates. The adapted assay, is based on the binding of porcine anti-guinea pig insulin antibodies to microtiter plates by IRMA method (16). Serum Leptin level: was measured by a commercially available ELISA kit (ALEXIS San Diego, USA).The microtiter bores are painted with a monoclonal antibody targeted towards a unique antigenic site on a Leptin molecule. An aliquot part of patient sample containing endogenous Leptin is incubated in the painted well with a specific rabbit anti-Leptin antibody. After incubation the unbound material is washed off and a Peroxidase Enzyme Complex is incorporated for determination of the bound Leptin. Serum levels of IL-6, TNF-α, and CRP were determined using reagents from BD Biosciences Pharmingen, California, USA. The result of serum insulin were then used for calculation of HOMA-IR (homeostatis model assessment: fasting glycemia* fasting insulin/22.5) (16).

Statistical analysis:

The data were analyzed using the statistical package for the Social Sciences Software (version 23.0; SPSS Inc., Chicago, IL) package. Independent Student's *t*-test was used to test the differences in the mean values for the continuous variables. Chi-square test was used to test the differences in the proportion of the categorical variables. The Pearson correlation coefficient (r) was used to determine the correlation between variables. Statistical significance was set at $P < 0.05$.

Results

This study was conducted on forty men and sixty women with the metabolic syndrome with the mean age of 47.22 ± 4.77 years matched for age and sex with controls. Table1 show the demographic characteristics of the study participants.

Table 1: Demographic data for patients and controls:

Demographic data	Patients	Controls	P value
Sex [No. (%)] **Male** **Female**	 **40(40%)** **60(60%)**	 **20(40%)** **30(60%)**	**0.146**
Age (years) **Mean ± SD**	**47.22± 4.77**	**46.48 ± 4.41**	**0.427**

This table shows no statistically significant difference between patients and controls as regard age and sex.

The baseline clinical characteristics of our participants are shown in "table 2". There were statistically significant difference between subjects with the metabolic syndrome and controls as regard to smoking history, systolic blood pressure, diastolic blood pressure, waist circumference, body mass index, and waist-hip ratio. For all the *p* was0.0001.

Table 2: Clinical characteristics for patients and controls

Clinical characteristics	Mean ± SD		t	P value
	Metabolic syndrome (Number=100)	**No metabolic syndrome (Number=50)**		
Smoking	**0.3 ± 0.460**	**0.02 ± 0.141**	**3.988**	**0.001***
SBP (mmHg)	**136.3 4± 9.877**	**112.96 ± 6.067**	**16.379**	**0.001***
DBP (mmHg)	**89.30 ± 7.015**	**62.42 ± 4.531**	**22.589**	**0.001***
WC (Cm)	**106.48 ± 10.88**	**84.83 ± 0.09**	**18.240**	**0.001***
BMI (Kg/m2)	**30.48 ± 4.54**	**24.37 ± 10.89**	**20.440**	**0.001***
WHR	**0.88 ± 0.04**	**0.83 ± 0.05**	**7.614**	**0.001***

*Statistically significant. SBP = Systolic blood pressure. DBP = Diastolic blood pressure. WC = Waist circumference. BMI = Body mass index. WHR = Waist: hip ratio. SD = Standard deviation.

The baseline laboratory characteristics of our participants are shown in "table 3". There were statistically significant difference between subjects with the metabolic syndrome and controls as regard to serum insulin, high density lipoprotein cholesterol (HDL-C), HOMA-IR, Leptin, C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α), but there were no statistically significant difference between subjects with the metabolic syndrome and controls as regard to plasma fasting blood sugar, serum triglycerides, total cholesterol, and low density lipoprotein cholesterol (LDL-C). The age- and sex-matched cases and controls differed in some of the metabolic syndrome parameters. The plasma levels of Leptin, CRP and inflammatory markers (IL-6, TNF-α) were significantly higher in the group with the metabolic syndrome.

Table 3: Laboratory and inflammatory markers in patients and controls

Characteristics	Mean ± SD		t	P value
	Metabolic syndrome	**No metabolic syndrome**		
Glucose (mg/dl)	**107.66 ± 9.535**	**90.0 ±10.0**	**8.879**	**0.804**
Insulin (mIU/ml)	**13.051 ± 2.034**	**7.020 ± 2.08**	**25.129**	**0.001***
Triglyceride (mg/dl)	**153.88 ± 10.275**	**143.46 ± 8.701**	**5.338**	**0.722**
Total cholesterol (mg/dl)	**216.140 ± 15.109**	**162.680 ± 17.406**	**16.341**	**0.960**
HDL (mg/dl)	**34.500 ± 2.957**	**54.220 ± 4.661**	**-30.990**	**0.008***
LDL (mg/dl)	**110.860 ± 9.149**	**92.640 ± 4.623**	**12.484**	**0.909**
IR	**3.867 ± 0.753**	**1.540 ± 0.494**	**30.852**	**0.001***
CRP (mg/l)	**23.28 0± 12.673**	**4.640 ± 1.025**	**10.041**	**0.003***
IL-6 (Pg/ml)	**11.960±1.897**	**5.405 ± 1.970**	**38.167**	**0.001***
TNF-α (Pg/ml)	**8.560 ± 2.397**	**4.689 ± 1.672**	**28.083**	**0.001***
Leptin (ng/mI)	**22.424 ± 2.545**	**10.600 ± .728**	**41.241**	**0.001***

*Statistically significant. HDL = High density lipoprotein. LDL = Low density lipoprotein. CRP = C-reactive protein. IR= Insulin resistance. IL-6 = Interleukin 6. TNF-α = Tumor necrosis factor-alpha

There was statistically significant correlation between CRP with systolic blood pressure, diastolic blood pressure, waist circumference, body mass index, HDL-C, LDL-C, triglyceride, HOMA-IR, Leptin, IL-6 and TNF-α as shown in "table 4".

Table 4: Correlation between CRP and parameters of metabolic syndrome

Parameters of metabolic syndrome	CRP	
	r	**P value**
SBP(mmHg)	**0.472**	**0.001***
DBP(mmHg)	**0.423**	**0.001***
WC (Cm)	**0.274**	0.006*
BMI (Kg/m2)	0.794	0.001*
Glucose (mg/dI)	- .037	**0.718**
Triglyceride (mg/dI)	**-0.213**	**0.033***
Total cholesterol (mg/dI)	0.147	**0.144**
HDL(mg/dI)	0.210	**0.036***
LDL (mg/dI)	0.223	**0.025***
IR	0.718	**0.001***
IL-6 (Pg/ml)	0.538	**0.001***
TNF-α (Pg/ml)	0.537	**0.049***
Leptin(ng/mI)	0.275	**0.006***

*Statistically significant. r= Correlation coefficient. SBP = Systolic blood pressure. DBP = Diastolic blood pressure. WC = Waist circumference. BMI = Body mass index. WC = Waist circumference. HDL = High density lipoprotein. LDL = Low density lipoprotein. CRP = C-reactive protein. IR= Insulin resistance. IL-6 = Interleukin 6. TNF-α = Tumor necrosis factor-alpha.

There was statistically significant correlation between plasma Leptin concentration with body mass index (BMI), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood sugar (FBS), homeostasis model assessment for insulin resistance (HOMA-IR), glycosylated hemoglobin (HbA1C), total cholesterol, high density lipoprotein cholesterol (HDL), C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and serum insulin but no significant correlation with both triglyceride and LDL-C levels as shown in "table 5".

Table 5: Correlation between serum Leptin with parameters of metabolic syndrome and inflammatory markers

Leptin		
Parameters	**r**	**P value**
BMI (Kg/m2)	0.431	0.001*
WC (Cm)	0.387	0.001*
SBP (mmHg)	0.212	0.035*
DBP (mmHg)	0.365	0.001*
FBS (mg/dI)	0.438	0.001*
IR	0.526	0.001*
HbA1c (%)	0.984	0.001*
Triglyceride (mg/dI)	-0.088	0.386
Total cholesterol (mg/dI)	0.474	0.001*
HDL (mg/dI)	-0.298	0.003*
LDL (mg/dI)	-0.168	0.095
CRP (mg/I)	0.275	0.006*
IL-6 (Pg/ml)	0.506	0.001*
TNF-α (Pg/ml)	0.648	0.001*
Insulin (mIU/ml)	0.515	0.001*

*Statistically significant. r= Correlation coefficient. SBP = Systolic blood pressure. DBP = Diastolic blood pressure. BMI = Body mass index. WC = Waist circumference. HDL = High density lipoprotein. LDL = Low density lipoprotein. FBS= Fasting blood sugar. CRP = C-reactive protein. IR= Insulin resistance. IL-6 = Interleukin 6. TNF-α = Tumor necrosis factor-alpha.

Discussion

The metabolic syndrome is clustering of cardiovascular risk factors in an individual, which includes abdominal obesity, hypertension, glucose intolerance, hyperlipidemia, and insulin resistance, and is associated with an increased liability for diabetes and cardiovascular disease (17). Inflammation plays a crucial role both in the evolving of insulin resistance and metabolic syndrome (18). The development of a strong biomarker that can previse metabolic syndrome rather than individual variable examination features will be crucial from a population viewpoint in recording, screening the natural history of the disease, and assessing the therapeutic intervention responses.

This study determined a significantly high level of interleukin-6 (IL-6), tumor necrosis factor- α (TNF-α) and C-reactive protein (CRP) in the metabolic syndrome subjects if compared to the controls without metabolic syndrome. Our findings were similar to studies done by Indulekha *et al* (19) and Choi *et al* (20) that reported significantly elevated high-sensitivity CRP levels in Asian Indians and elderly Korean women with impaired glucose tolerance compared to controls with normal glucose tolerance and also reported equivalent levels of interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α)in subjects with and without impaired glucose tolerance. Kitsios *et al* (21) reported an elevated IL-6 levels in obese young adults but comparable TNF-α levels in obese and normal weight young adults. The different study inhabitants, the different measures for defining metabolic syndrome as fortified by different organizational bodies (3, 22, 23), and the different varieties of dys-metabolic features that categorize the syndrome may account for some of the observed differences from these studies. From these studies, a recurrent component, however, is an increase in the concentration of one or more bio-markers of inflammation in relation to the various parameters that define the syndrome.

The cause for the inflammatory cascade in metabolic syndrome is not yet fully understood. An explanation may be that larger adipose tissue mass in obesity leads to increased release of IL-6 and TNF-α into the circulation which in turn stimulates excessive production of CRP by the liver (10, 11). Another theory is that insulin resistance (IR) itself is responsible for the higher production of these inflammatory cytokines (10, 11). These reports verify our findings in this study of a positive association between CRP with both waist circumference, and body mass index(surrogate markers for abdominal obesity), and IR in the metabolic syndrome. The finding of an elevated CRP levels and the correlation between CRP (a marker of inflammation) and the metabolic syndrome components of waist circumference, IR, high LDL and low HDL (markers of cardiovascular risk) in this study, supports results from other studies of the importance of an elevated levels of CRP as a significant new feature associated with the metabolic syndrome (10, 11).

Our study showed a significant high serum Leptin and Insulin hormone levels in metabolic syndrome group if compared to the control group. An extra evidence supports that insulin can modulate Leptin expression. This is most evident from experimental studies on isolated adipocytes, which revealed that in vitro insulin obviously promotes the mRNA expression and secretion of Leptin in cultured rat and human adipocytes. Another obvious possibility, glucose metabolism looks to be an important determinative of Leptin expression and secretion. In human experiments, elevated insulin level induced by clamp techniques leads to an elevation in Leptin concentration levels(24). One report on a patient with pancreatic islet cell insulin-secreting tumor (insulinoma) revealed significantly elevated Leptin levels during chronichyperinsulinism, and both hormones dropped after surgical removal (25).

Elevated Leptin concentrations may in part be altered by hyperinsulinism or impaired insulin sensitivity. This in agreement with our results where there was a significant correlation between serum Leptin level and insulin resistance. Leptin positively correlated with body mass index (BMI), waist circumference (WC), and both SBP and DBP in metabolic syndrome group. These results corroborate with Omar et al (26) who found that Leptin concentrations were high in both obese and diabetic obese group and showed a direct positive relation with BMI and waist circumference. Shankar and Xiao (27) revealed that, elevated levels of plasma Leptinare associated with elevated blood pressure in both genders in a representative sample of adults. In this study, Leptin showed significant correlation with FBS, HbA1C, and HOMA-IR. Martins et al. (28) concluded that elevated Leptin level, particularly in obese individuals, should be taken as an alarming sign of energy imbalance, poor diet, hyperinsulinism, insulin resistance, and/or changes in other metabolic risk factors that are strongly associated with cardiovascular disease and type-2 diabetes mellitus (T2DM). Leptin receptors are present on human liver cells, and Leptin was seen to modify a diverse of induced insulin activities in these cells. Leptin counteracts insulin signaling by reducing insulininduced tyrosine phosphorylation of Insulin Receptor Substrate (IRS), it augments phosphoenolpyruvate-carboxykinase and diminishes glucokinase expression leading to increased gluconeogenesis and decreased glycolysis (29). The hepatic effects of high Leptin levels may thus contribute to hepatic insulin resistance. An approximate number of studies revealed that Leptin is capable of to adjust insulin action (on glucose consumption and/or lipogensis) in both adipocytes and myocytes. Other studies establish no effect on peripheral glucose uptake (30). Leptin may work at various levels inside the cell, including transcription to membrane permeability to suppress synthesis of insulin as well as its secretion. Functional Leptin receptors also exist on insulin-secreting pancreatic β-cells (31). The insulin reducing effect of Leptin intake could thus be initiated throughout these receptors. Lately, an uninterrupted effect of Leptin on insulin transcriptiongene in pancreatic β-cells has been observed, with a diminution of preproinsulin mRNA by 50% (32). On the other side, defective insulin sensitivity may influence an increased insulin levels and led to elevatedLeptin levels by an abnormal modulation of the hypothalamic Leptin receptors or the subsequent satiety response to Leptin. Insulin resistance has been evaluated as a potential risk factor for coronary heart disease (CHD) in the general population (33). Our results in correspondence with these findings, where a positively significant correlation was observed between insulin and Leptin. According to the results of lipid profile in the current study, there was a positively significant correlation between Leptin and serum total cholesterol (TC) with a negatively significant correlation with high density lipoprotein cholesterol (HDL). Hiroshi et al. observed that Leptin was correlated positively with SBP, DBP, FPG, TC, TG, LDL-C and negatively correlated with HDL-C (34).

Leptin may also have a role in the immune response via the stimulation of T-helper cell proliferation and production of pro-inflammatory cytokines as IL-6 and TNF-α which induce liver CRP synthesis. In addition, Leptin formed in fat cells may directly influence production of IL-6, leading to in further modulation of CRP production in liver cells (35). In our study, there was a highly significant correlation between Leptin with both TNF-α and IL-6 indicating that these cytokines directly correlated with the presence of metabolic syndrome. Thus, serum Leptin may be considered as a proinflammatory cytokine as it upregulates TNF-α and IL-6 that are associated with IR in DM2 and may be used as an incorporated marker of adiposeness, insulin unresponsiveness, and vascular dysfunction beneficial for cardiovascular risk assessment in clinical practice, and may have an important purpose in subclinical inflammatory condition in metabolic syndrome (36).

The mechanisms linking Leptin and CRP are not clear. Fat tissue is the origin of distributing plasma Leptin (7). CRP is formed by hepatocytes, mainly under the effect of the proinflammatory cytokines, principally IL-6 (21). The hepatic synthesis of CRP can also be influenced by other proinflammatory cytokines such as interleukin-1, and TNF-α. Adipocyte serve as an important source of circulating IL-6 (35), also present and express TNF- α (21, 36). Hence, as adipocytes a main source for Leptin and inflammatory cytokines leading to more CRP synthesis, thus, these may clarify in part the inter-relation between CRP and Leptin. Furthermore, IL-1, IL-6, and TNF-α, that lead to an elevation in CRP, may act promptly on adipocytes to rise Leptin secretion in situations of acute inflammatory conditions (25–28), additionally encouraging adipose tissue as a possible common pathway leading to the Leptin–CRP inter-relationship. Nevertheless, the strong interaction between Leptin and CRP in the present study was dependent on several means of adiposity (e.g., BMI and waist-to-hip ratio). Thus, another explanation may be that Leptin may modulate CRP levels by a direct or indirect way through the immune system. First, Leptin can really prompt the secretion of different cytokines, including IL-6 (21). Second, IL-6 influences CRP. Third, the Leptin receptor has been demonstrated to have signaling properties for IL-6 –type cytokine receptors (28, 36). It is believable then that Leptin may work through IL-6, or possibly even via the Leptin receptor, to modulate CRP production. Our data may increment the probability that Leptin may act to raise levels of CRP in individuals with metabolic syndrome and may lead to a high cardiovascular mortality, insulin resistance and type 2 diabetes mellitus.

The individuals with both metabolic syndrome and inflammatory arthritis had low levels of CRP and other inflammatory cardiovascular risk parameters following therapy with a TNF-α blocking agent (37). This may clarify the purpose of inflammatory cascade in the pathogenesis of metabolic syndrome and its probability for therapeutic intervention for metabolic syndrome and its related health sequelae.

In conclusion, this study reveals an increase in the mediators of inflammation in subjects with metabolic syndrome. It also reports a significant correlation between Leptin and CRP with some parameters of the metabolic syndrome. Thus, in this study Inflammation may have a critical role in the pathophysiology of metabolic syndrome through modulation of Leptin and proinflammatory cytokines.

References

1. Zimmet P, Alberti KGMM, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S; IDF Consensus Group. The metabolic syndrome in children and adolescents – an IDF consensus report. Pediatric Diabetes 2007 Oct; 8(5): 299-306.
2. Alberti KGMM, Zimmet PZ, Shaw JE. The metabolic syndrome—a new world-wide definition from the International Diabetes Federation Consensus. Lancet 2005; 366: 1059-1062.
3. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) JAMA. 2001; 285:2486–97.
4. Lutsey PL, Steffen LM, Stevens J – Dietary intake and the developmentof the metabolic syndrome: theAtherosclerosis Risk in Communities study. *Circulation* 2008; 117:754-761.
5. Ninomiya JK, L'Italien G, Criqui MH, Whyte JL, Gamst A, Chen RS. Association of the metabolic syndrome with history of myocardial infarction and stroke in the Third National Health and Nutrition Examination Survey. Circulation. 2004; 109:42–6.

6. Klein BE, Klein R, Lee KE. Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. Diabetes Care. 2002; 25:1790–4.
7. J´equier E. Leptin signaling, adiposity, and energy balance. Lipids and insulin resistance: the role of fatty acid metabolism and fuel partitioning. Ann NY Acad Sci 2002; 967: 379–388.
8. Moran O, Phillip M. Leptin: obesity, diabetes and other peripheral effects—a review. Pediat Diab 2003; 4: 101–109.
9. Ghantous CM, Azrak Z, Hanache S, Abou-Kheir W, Zeidan A. Differential Role of Leptin and Adiponectin in Cardiovascular System. International journal of endocrinology. 2015; 2015: 534320.
10. Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: A comprehensive perspective based on interactions between obesity, diabetes, and inflammation. Circulation. 2005; 111:1448–54.
11. Sharma P. Inflammation and the metabolic syndrome. Indian J Clin Biochem. 2011;26:317–8
12. Jiang CQ, Lam TH, Liu B, Lin JM, Yue XJ, Jin YL, et al. Interleukin-6 receptor gene polymorphism modulates interleukin-6 levels and the metabolic syndrome: GBCS-CVD. Obesity (Silver Spring) 2010; 18:1969–74.
13. Wannamethee SG, Whincup PH, Rumley A, Lowe GD. Inter-relationships of interleukin-6, cardiovascular risk factors and the metabolic syndrome among older men. J Thromb Haemost. 2007; 5:1637–43.
14. Moreira PF, Dalboni MA, Cendoroglo M, Santos GM, Cendoroglo MS. Postprandial interleukin-6 response in elderly with abdominal obesity and metabolic syndrome. J Nutr Health Aging. 2013; 17:206–10.
15. Langenberg C, Bergstrom J, Scheidt-Nave C, Pfeilschifter J, Barrett-Connor E. Cardiovascular death and the metabolic syndrome: Role of adiposity-signaling hormones and inflammatory markers. Diabetes Care. 2006; 29:1363–9.
16. MATTHEWE DR, HOSKER JP, RUDENSKI AS, NAYLOR BA, TREACHER DF, TURNER RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28: 412-419, 1985.
17. Reaven GM. The insulin resistance syndrome: definition and dietary approaches to treatment. Ann Rev Nutr. 2005; 25:391-406.
18. Devaraj S, Rosenson RS, Jialal I. Metabolic syndrome: an appraisal of the pro-inflammatory and procoagulant status. Endocrinol Metab Clin North Am. 2004; 33:431-53.
19. Indulekha K, Surendar J, Mohan V. High sensitivity C-reactive protein, tumor necrosis factor-a, interleukin-6, and vascular cell adhesion molecule-1 levels in Asian Indians with metabolic syndrome and insulin resistance (CURES-105) J Diabetes Sci Technol. 2011;5:982–8.
20. Choi KM, Lee J, Lee KW, Seo JA, Oh JH, Kim SG, et al. Comparison of serum concentrations of C-reactive protein, TNF-alpha, and interleukin 6 between elderly Korean women with normal and impaired glucose tolerance. Diabetes Res Clin Pract. 2004; 64:99–106.
21. Kitsios K, Papadopoulou M, Kosta K, Kadoglou N, Chatzidimitriou D, Chatzopoulou F, et al. Interleukin-6, Tumor necrosis factor a and metabolic disorders in youth. Int J Endocrinol Metab. 2012; 2:120–7.
22. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009; 120:1640–5.
23. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998; 15:539–53.
24. Boden G, Chen X, Kolaczynski JW, Polansky M (1997) Effects of prolonged hyperinsulinemia on serum Leptin in normal human subjects. J Clin Invest 100: 1107-1113.
25. Korbonits M, Trainer PJ, Little JA, Edwards R, Kopelman PG, et al. (1997) Leptin levels do not change acutely with food administration in normal or obese subjects, but are negatively correlated with pituitary-adrenal activity. Clin Endocrinol (Oxf) 46: 751-757.
26. Adil Omar Saeed Bahathiq (2010) Relationship of Leptin Hormones with Body Mass Index and Waist Circumference in Saudi Female Population of the Makkah Community. The Open Obesity Journal 2: 95-100.

27. Shankar A, Xiao J (2010) Positive relationship between plasma Leptin level and hypertension. Hypertension 56: 623-628.
28. Martins Mdo C, Lima Faleiro L, Fonseca A (2012) [Relationship between Leptin and body mass and metabolic syndrome in an adult population]. Rev Port Cardiol 31: 711-719.
29. Cohen B, Novick D, Rubinstein M (1996) Modulation of insulin activities by Leptin. Science 274: 1185-1188.
30. Liu L, Karkanias GB, Morales JC, Hawkins M, Barzilai N, et al. (1998) Intracerebroventricular Leptin regulates hepatic but not peripheral glucose fluxes. J Biol Chem 273: 31160-31167.
31. Kieffer TJ, Heller RS, Habener JF (1996) Leptin receptors expressed on pancreatic beta-cells. Biochem Biophys Res Commun 224: 522-527.
32. Seufert J, Kieffer TJ, Habener JF (1999) Leptin inhibits insulin gene transcription and reverses hyperinsulinaemia in Leptin-deficient ob/ob mice. Proc Natl Acad Sci U S A 96: 674-679.
33. Jeanrenaud B (1994) Central nervous system and peripheral abnormalities: clues to the understanding of obesity and NIDDM. Diabetologia 37 Suppl 2: S170-178.
34. Hiroshi H, Ikuo S, Toshihide K, Minako T, Hiroshi K, et al. (2001) Relationships between baseline serum Leptin levels and 2-year changes in body mass index, blood pressure and metabolic parameters in Japanese male adolescents and middle-aged men. Clin Sci 100: 145-150.
35. Balasoiu M, Balasoiu AT, Stepan AE, Dinescu SN, Avramescu CS, Dumitrescu D, et al. Proatherogenic adipocytokines levels in metabolic syndrome. Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie. 2014; 55: 29-33.
36. Patricio LJ, Diego GA, Jose LL, Cristina LL, Javier MO, Andrea GR and Stefany TC, et al. The role of Leptin/adiponectin ratio in metabolic syndrome and diabetes**.** Horm Mol Biol Clin Invest 2014; 18(1): 37–45.
37. Bernstein LE, Berry J, Kim S, Canavan B, Grinspoon SK. Effects of etanercept in patients with the metabolic syndrome. Arch Intern Med. 2006; 166:902–8.

Access this Article in Online	
Quick Response Code	Website: www.ijarbs.com Subject: Medicine
DOI:10.22192/ijarbs.2018.05.02.009	

How to cite this article:
Arafat Kassem, Mohamed Rashed. (2018). Study of the Plasma levels of Leptin and inflammatory cytokines in Egyptians with metabolic syndrome. Int. J. Adv. Res. Biol. Sci. 5(2): 82-90.
DOI: http://dx.doi.org/10.22192/ijarbs.2018.05.02.009