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SERUM ADIPONECTIN AND LEPTIN LEVELS AND THEIR RELATIONS WITH METABOLIC SYNDROME

Biochemistry

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ABSTRACT

Background & objectives: Adiponectin is an abundantly expressed adipocyte-specific protein, whose level is decreased in obesity, and which appears to be a key participant in developing inflammation, insulin resistance and metabolic syndrome (MetS). We examined whether the relationship between adiponectin and leptin, insulin resistance and MetS was independent of obesity.
Materials and Methods: We studied 200 subjects, with Metabolic syndrome, diagnosed by International Diabetes Federation criteria and 200 healthy control subjects, age between 25-65 years. Clinical evaluation included anthropometry, Waist circumference, Body Mass Index and waist-to-hip ratio were calculated. The blood pressure systolic and diastolic, was also measured. Circulating levels of fasting glucose, total cholestero, high-density lipoproteins, adiponectin, leptin and free fatty acids were determined. Serum leptin, adiponectin and free fatty acids were estimated by sandwich ELISA method. **Results:** In our study, Subjects with the MetS had lower adiponectin and higher leptin levels ($P<0.0001$ for both variables) compared with individuals without the MetS. Adiponectin was significantly correlated with Age, BMI, WC, Waist-Hip ratio, Fasting blood sugar, Total Cholesterol, Triglycerides, High-density lipoprotein (HDL) cholesterol, Leptin, Free fatty acid and also highly significant ($P<0.0001$) for all variables. **Conclusion:** Serum concentrations of Leptin are associated with central body fat distribution. Insulin resistance and Adiponectin is associated with Dyslipidemia and these all disorders may ultimately lead to metabolic syndrome. Adiponectin, Leptin levels, Free fatty acid could be used as markers of metabolic syndrome development in adolescents. Obesity and related disturbances put these adults at a higher cardiovascular risk. Hence there is an urgent need for public health measures to prevent the ongoing epidemic of diabetes and CVD.

KEYWORDS

Adiponectin, Leptin, Free Fatty Acid and Metabolic Syndrome.

Introduction

Metabolic syndrome is a cluster of atherosclerotic cardiovascular disease risk factors manifested as central obesity, insulin resistance, dyslipidaemia and hypertension.1 Central obesity appears to play an important role in metabolic syndrome and insulin resistance. Thus, the International Diabetes Federation (IDF) has suggested that central obesity is the main risk factor for metabolic syndrome.2 Central adiposity may be linked to insulin resistance and metabolic syndrome through the production of various adipocyte-derived cytokines, known as adipokines.3 It has been suggested that disruption of the secretion of adipokines has many metabolic consequences.4,5

It is well recognized that the adipose tissue is not only a storage site for lipids but also an active endocrine organ.6 In obese persons, excess uptake of carbohydrates and lipids may lead to cell dysfunction of adipocytes. Due to such an energy imbalance, abnormal adipose-derived hormones release influences not only gain of body weight but also development of chronic inflammation, insulin resistance, metabolic syndrome, diabetes, and cardiovascular disease.7-9 Adiponectin and leptin are two major adipose-derived hormones that are secreted only by adipose tissue. Adiponectin had been shown to improve glucose metabolism, stimulate fatty acid oxidation and possessed anti-inflammatory and anti-atherogenic actions.11-13 Leptin controls food intake and stimulates energy expenditure and circulating leptin levels proportional to body fat.10 However, high circulating concentrations of leptin are usually found in obese people without weight loses because of leptin desensitization.14,15 It is also well recognized that there is a significant inverse relationship between blood adiponectin and leptin levels that independent of age, BUN, blood pressure, body composition, lipids and in- sulin resistance.16

In this study, we analyzed serum adiponectin and leptin levels and their relationship with anthropometric features and metabolic syndrome trials. Since the distur- bance of adipose-derived hormones is usually present in metabolic syndrome, evaluation of circulating leptin and adiponectin is helpful for the assessment of metabolic dysfunction, especially when the lacks of feasibility to metabolic syndrome criteria measurements.

MATERIALS AND METHODS

The study was a case-control analytic cross-sectional study. This study was carried out at Department of Biochemistry, in collaboration with the Department of General Medicine at S.P. Medical College and Associated group of P.B.M. Hospitals, Bikaner. All participants completed a medical history form and provided informed consent. Study was included 400 subjects. These subjects were divided into two groups. Group I/ involved as the prevalence of Metabolic syndrome in an adult population, consist of 200 subjects, male 126 (63%) and female 74 (37%) with MS diagnosed by International Diabetes Federation (IDF).17 criteria and 200 healthy, male 114 (57%) and female 86 (43%) and age between 25-65 years control subjects. Present study was done from June 2015 to June 2018.

Case selection criteria

Inclusion Criteria: International Diabetes Federation (IDF) 200517 criteria for Metabolic Syndrome as follows:

Exclusion Criteria:

Serious ill/moribund patient, Severe hepatic or renal disease, Cancer, Stroke, Pregnant women, Autoimmune diseases, Familial hyperlipidemia and patients taking lipid lowering medication and with a history of abdominal surgery, which could have an impact on abdominal fat distribution, were excluded from the study.

Blood Sample collection:- Venous blood samples were collected in test tube with aseptic precautions. After 2 hours of collections sample was centrifuged at 3000 rpm for 5minutes. Serum was separated and collected in polythene tube with cork. The sera with no sign of hemolysis used for the analysis of all biochemical parameters.

Adiponectin Estimation

Serum Adiponectin concentration was measured using ALPCO, USA, High Molecular Weight (HMW) & Total Adiponectin ELISA kit for research use only.

Leptin Estimation

Serum Leptin concentration was estimated using Diagnostic Automation, Inc., USA, Microwell ELISA kit for research use only.

Free Fatty Acid Serum Free Fatty Acid concentration was estimated using SIGMA ALDRICH, USA, Free Fatty Acid Quantitation kit, ELISA kit for research use only.

Results

Table 1 shows the anthropometric measurements of the subjects of both metabolic syndrome (n=200) and non-metabolic syndrome (n=200). As expected, mean levels of BMI, Waist Circumference (WC), Hip Circumference (HC), Waist to Hip Ratio (Wc/Hc), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) showed marked difference and were statistically significantly increased (P<0.0001) in both the groups. Biochemical parameters of the individuals studied in the present study are given in the (Table 2). Glucose (FBS), Post Parandial blood glucose (PPBS), Triglycerides (TG), Total Cholesterol (TC), LDL-C, VLDL-C, Leptin and Free Fatty Acid level were significantly increased (P<0.0001)(Table no. 3 & 4) and HDL-C, Adiponectin levels were significantly reduced (P<0.0001))(Table no.1) in obese subjects with and without MS compared to controls.

Discussion

Those participants suffering from the metabolic syndrome had higher levels of leptin, higher levels of inflammatory markers and lower levels of serum adiponectin. In correlation analysis, adiponectin and leptin were both correlated with inflammatory markers. It is known that dysfunctional adipocytes usually release IL-6 and TNF-alpha that stimulate leptin secretion and inhibited adiponectin synthesis. Furthermore, leptin positively modulates while adiponectin negatively modulates CRP.14,15 In other studies, both leptin and adiponectin were independently associated with CRP concentrations in males.16 We also found that adiponectin was correlated with hs-CRP in females and leptin was correlated with selecting in males. Therefore the detection of information about the inflammation reaction cause by the dysfunctional adipocytes.

Leptin and adiponectin play important roles in energy expenditure, glucose metabolism, fatty acid oxidation and insulin action. Abnormal serum levels of leptin and adiponectin appear to be signals of metabolic syndrome occurs. Zhuo et al. showed that leptin and leptin to adiponectin ratio are better biomarkers for metabolic syndrome than adiponectin. However, they also showed the odds ratio between leptin and metabolic syndrome decreased substantially after the adjustment for age and BMI.16 In Galletti's study, leptin was a significant predictor for the risk of the metabolic syndrome during an average follow-up period of eight years.18 In this study we found that adiponectin had a better diagnostic ability than leptin did. Furthermore, logistic regression showed that only adiponectin was a risk factor for metabolic syndrome independent of age, waist circumference and BMI. Gannage-Yared et al. reported that the relationship of leptin to lipid profile is mainly mediated by BMI.19 Their findings are consistent with us. These results suggest that the relationship be- tween leptin and the metabolic syndrome is mainly mediated by obesity.

Conclusion

In conclusion, circulating total adiponectin and HMW adiponectin levels were decreased and leptin levels were increased in subjects with metabolic syndrome and type 2 diabetes. In our results demonstrate a positive relationship between Adiponectin, Leptin levels, Free fatty acid and parameters of metabolic syndrome, including BP values in normotensive subjects with overweight/obesity. Serum concentrations of Leptin are associated with central body fat distribution. Insulin resistance and Adiponectin are associated with Dyslipidemia and these all disorders may ultimately lead to metabolic syndrome.

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Table:1

Comparison of Mean±SD of Anthropometric Parameters of the Metabolic Syndrome and without Metabolic Syndrome Control Subjects

Sr.No	Parameters	MetS Cases Mean±S.D (n= 200)	No MetS Control Mean±S.D (n= 200)	p-value
1.	Age (Years)	45.90± 11.50	44.89± 11.22	
2.	Body Weight (Kg)	76.46± 10.36	61.92± 11.75	0.0001
3.	BMI (kg/m2)	34.40± 3.33	23.80± 1.64	0.0001
4.	Waist circumference (cms)	93.39± 9.64	87.73± 8.16	0.0001
5.	Waist-Hip Ratio (WHR)	0.92± 0.07	0.829± 0.04	0.0001
6.	Systolic blood pressure (mm Hg)	151.0± 14.4	123.23± 6.70	0.0001
7.	Diastolic blood pressure (mm Hg)	86.89± 2.12	72.60± 4.40	0.0001

Figure:1 Comparison of Mean of Anthropometric Parameters of the Metabolic Syndrome and without Metabolic Syndrome Control Subjects

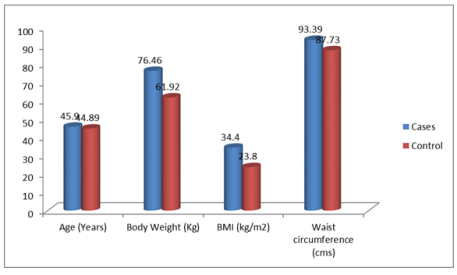


Table No.- 2

Comparison of Serum Adiponectin (µg/ml) of the Healthy control subjects and Metabolic Syndrome Subjects

S.No.	Values	Healthy control subjects (n=200)	Metabolic Syndrome Subjects (n=200)
1	Mean	7.48	5.131
2	Range	3.64- 10.88	3.1- 8.4
3	SD	1.48	1.304
4	T	16.86	
5	DF	398	
6	P-value	0.0001	

Figure No.- 2

Comparison of Serum Adiponectin (µg/ml) levels in Metabolic Syndrome subjects with Healthy control subjects

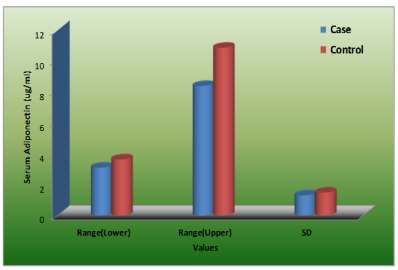


Table No.- 3 Comparison of Serum Leptin (ng/ml) of the Healthy control subjects and Metabolic Syndrome Subjects

S.No.	Values	Healthy control subjects (n=200)	Metabolic Syndrome Subjects (n=200)
1	Mean	5.301	12.28
2	Range	3.14- 11.23	6.2- 20.7
3	SD	1.85	4.17
4	T	21.63	
5	DF	398	
6	P-value	0.0001	

Figure No.- 3
Comparison of Serum Leptin (ng/ml) levels in Metabolic Syndrome subjects with Healthy control subjects

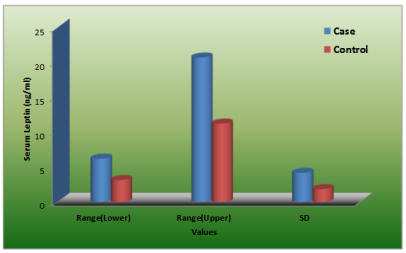
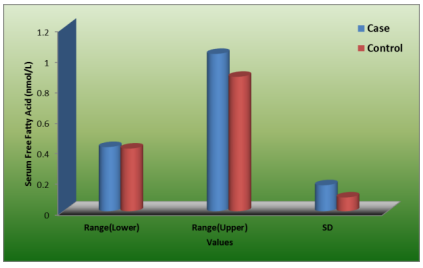


Table No.- 4 Comparison of Free Fatty Acid (nmol/L) of the Healthy control subjects and Metabolic Syndrome Subjects

S.No.	Values	Healthy control subjects (n=200)	Metabolic Syndrome Subjects (n=200)
1	Mean	0.625	0.85
2	Range	0.41- 0.88	0.42- 1.03
3	SD	0.09	0.17
4	T	34.74	
5	DF	398	
6	P-value	0.0001	

Figure No.- 4
Comparison of Serum Free Fatty Acid (nmol/L) levels in Metabolic Syndrome subjects with Healthy control subjects



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