Correlation of serum leptin with various components of metabolic syndrome

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Abstract

Background: Serum leptin may help in early identification of metabolic syndrome (MetS).
Objective: To establish the correlation of leptin levels with various components of metabolic syndrome, its levels were first measured and then its possible correlation was found out with each component of metabolic syndrome.
Methodology: This case-control study was conducted on 100 subjects (50 patients of MetS along with equal number of age and sex matched controls) in Pathology Department, Army Medical College, Military Hospital, Rawalpindi. Patients with a history of thyroid, hematological, liver and neoplastic diseases were excluded from this study. After getting information regarding the history, anthropometric indices of obesity were measured and required laboratory investigations were carried out to determine any correlation between serum leptin with metabolic syndrome components. Data was analyzed by using SPSS version 17.
Results: Laboratory investigations showed that MetS patients had elevated leptin levels of 12.98 ± 2.68 (ng/ml) as compared to 5.34 ± 1.84 (ng/ml) in controls (p value < 0.001). In correlation analysis, serum leptin showed a significant positive correlation with various components of metabolic syndrome like BMI (r; p value: 0.837; 0.001), WC (r; p value: 0.730; 0.001), WHR (r; p value, 0.855; 0.001), HOMA-IR (r; p value, 0.853; 0.001) and insulin levels (r; p value, 0.864; 0.001). TG exhibited a positive correlation with leptin (r; p value, 0.780; 0.001) as compared to inverse correlation exhibited by HDL (r; p value, 0.818; 0.001).
Conclusion: Metabolic syndrome patients not only showed significantly raised serum leptin levels but also this circulating leptin established a strong correlation with each component that fulfil the WHO criteria of metabolic syndrome.

Key words: Metabolic syndrome, Serum leptin, HOMA-IR.

Introduction

Metabolic syndrome is considered as the rising disease of 21st century.[1] The term MetS is a combination of various disorders including insulin resistance, hypertension and lipid disorder (increased triglycerides and decreased HDL-c).[2] General population has 17% to 25% prevalence of MetS, giving the strong evidence of interconnected risk factors like obesity and insulin resistance that contribute the major make up of MetS.[3] Unlike the European countries, MetS among the Asian population occur at a younger age.[4] Moreover, complications related to this syndrome manifest with decreased amount of adiposity.[5] A study has documented the prevalence of 16.3% and 48.2% in males and females respectively.[6]

The number of patients suffering with this syndrome are increasing day by day with a a greater risk of developing various metabolic abnormalities like diabetes mellitus and cardiovascular disorders.[7] Presence of just one condition does not indicate that the individual is suffering from MetS, however, suffering from more than one of these conditions enhance the risk of developing serious complications.[8] This combination of risk factors, that occur in an individual, suggest that there are some common pathways underlying their causes and pathophysiology.[9]

Leptin comes from a Greek word “leptos” which means “thin”. Out of many functions of leptin, appetite suppression is the top most, but its levels have been found significantly raised in obese individuals.[10] The sustained secretion of leptin from the adipose tissues result in leptin desensitization in obese people and this process is comparable to type-2 diabetic patients who suffer from insulin resistance in much the same way.[11]

One of the main effects of leptin in different parts of body is that it has been recognized as the underlying factor in causing insulin resistance in obesity. Moreover, leptin is a predisposing factor in obese people by modulating the immune response to

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atherosclerosis.[12] This adipose-derived hormone physically interacts with C-reactive protein, resulting in leptin resistance. Elevated serum leptin not only show a correlation with the various components of metabolic syndrome but also predict the risk of cardiovascular diseases.[13-15]
In this way, measuring the serum leptin levels and finding its association with its components will help in future to adopt preventive strategies to lower the risk of various complications associated with this syndrome.[14] The objective of the study was to assess the correlation of serum leptin with various components of metabolic syndrome.

Methodology

Study Design: Case control study. Setting of Study: Pathology Department, Military hospital, Rawalpindi. Study duration: One year. Sampling technique: Non-probability, convenience sampling. Inclusion Criteria: Metabolic syndrome patients fulfilling the WHO criteria. Exclusion Criteria: Patients with autoimmune, thyroid, inflammatory, liver, infectious and familial hyperlipidemia. Data collection: After getting the informed written consent, waist and hip circumference were measured in centimeters for calculating waist-to-hip ratio. BMI was calculated by the formula=Weight (kg)/Height (m^2). Ten ml of fasting venous blood sample was collected under sterile conditions. Routine investigations were performed on the same day, while the serum for insulin and leptin measurements was stored at -20 ^{0}C, until the biochemical analysis. Serum leptin was measured using DRG Leptin (Sandwich) ELISA kit for research use only. Plasma glucose, Triglyceride (TG) and High-density cholesterol (HDL-c) were measured by enzymatic colorimetric method on automated chemistry analyzer Selectra-E (vital scientific Netherlands). Low density cholesterol (LDL-c) was calculated by Friedewald formula:
LDL-c (mmol/l) = [TC]-[HDL-TG/2.2]
Insulin was measured on Access- 2 immunoassay (Beckman Coulter) based on principle of chemiluminescent immunoassay. Calculation of Insulin resistance was done using Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) =fasting plasma glucose × fasting plasma insulin/22.5.
Data Analysis: The data was analyzed on Statistical Package for the Social Sciences (SPSS) version 17. Insulin resistance and serum leptin in groups (cases and controls) were compared using independent t-test. Correlation analysis was done to establish the correlation of serum leptin levels with Insulin Resistance and Lipid profile. A *p*-value < 0·05 was considered to indicate statistical significance.

Results

Patients with MetS had elevated leptin levels of 12.98 ± 2.68 (ng/ml) as compared to 5.34 ± 1.84 (ng/ml) in controls (p value < 0.001) as shown in Figure I.

Figure I: Comparison of serum leptin levels among cases and controls

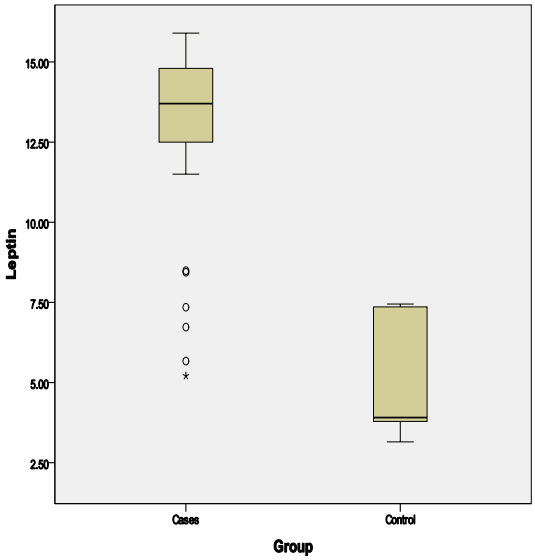

Table I: Correlation of serum Leptin with various components of MetS

Parameters	R-value	p-value
Basal metabolic rate (BMI, kg/m2)	0.837	0.001
Waist circumference (WC, cm)	0.730	0.001
Waist hip ratio (WHR)	0.855	0.001
Fasting plasma Insulin(μIU/ml)	0.864	0.001
HOMA-IR	0.853	0.001
Serum Triglyceride (TG,mmol/l)	0.780	0.001
Plasma High density lipoprotein cholesterol (HDL,mmol/l)	- 0.818	0.001

We have demonstrated that serum leptin correlated

significantly with various components of the metabolic syndrome. The correlation between leptin and various indices of obesity was as follows. BMI (r; p value: 0.837; 0.001), WC (r; p value: 0.730; 0.001), WHR (r; p value, 0.855; 0.001), HOMA-IR was (r; p value, 0.853; 0.001) and fasting insulin levels (r; p value, 0.864; 0.001). TG exhibited a positive correlation with leptin (r; p value, 0.780; 0.001) as compared to inverse correlation exhibited by HDL (r; p value, -0.818; 0.001).

Discussion

In our study serum leptin levels correlated significantly with MetS components such as obesity indices (BMI, WC, WHR), insulin resistance, dyslipidemia and fasting insulin (positive correlation with TG, while inverse correlation with HDL) as seen in several other studies.The MetS patients in the present study with BMI >27.4 kg/m^2 had higher leptin levels and showed a highly significant positive correlation (r = 0.837, P = 0.001) between serum leptin and insulin resistance when compared to non-obese control group (BMI < 23.0 kg/m^2). The serum leptin levels were directly related to body mass index which is an expression of obesity. As the BMI increases, the serum leptin and insulin resistance also increase. In obesity, it is generally expected that serum leptin levels would be low, as in obesity but paradoxically they are high.[15] This suggests that adult onset obesity is due to environmental factors like diet and sedentary life style and not due to genetically deficient leptin levels leading to unresponsiveness of satiety center to high circulating levels of leptin.[13] Most of the obese individuals have high levels of leptin because of their large fat mass, but they do not properly respond to these increased leptin levels.[16] This under-responsiveness to leptin, due to environmental factors has given rise to the idea that obesity is associated with a state of relative leptin resistance similar to the insulin resistance of type-2 diabetes.[17,18] The case group (MetS patients) of this study have increased waist circumference of 51.72 cm as compared to control group of 36.20 cm and also had a positive correlation with serum leptin levels (r = 0.730, p= <0.001). This association showed similarity with another study that also suggests that waist circumference indicate the amount of fat which has been accumulated in the body organs.[19] Infact, WCgives the explanation of link between adiposity and increased mortality rate as it indicates the metabolically active fat in the body.[20]

Values of insulin resistance vary among various ethnic groups and play a very important role in diagnosing the prediabetic patients.[21] In this study, the subjects in MetS group had hyperinsulinemia (FPI 28.39 ± 1.67; µIU/ml when compared with non-obese group (FPI 11.85 ± 1.14; µIU/ml). Moreover, insulin resistance (HOMA-IR) was measured from fasting blood samples. Infect, elevated fasting insulin levels reflect both decreased insulin sensitivity and decreased insulin secretion and is a potent risk factor of diabetes mellitus (type-2). Preventive measures like weight reduction should be adopted that will improve insulin resistance and prevent the development of type-2 diabetes mellitus.[22]

In metabolic syndrome, the main underlying pathophysiology is the resistance to the actions of insulin on carbohydrate metabolism. In this way, IR forms the basis of hyperinsulinemia and also leads to glucose intolerance, elevated triglyceride levels, and decreased HDL-c.[23] Moreover, fat deposition in liver is also associated with insulin resistance.[24] In 2009, a study established a strong relationship between obesity and IR and also explained that expanded dysfunctional adipose tissue mass not only becomes insulin resistant leading to ectopic fat deposition in liver and skeletal muscles but also acts as a source of secreting adipocytokines.[25]

In this study, a state of hyperleptinemia and a strong correlation between serum leptin level and insulin resistance in MetS (r = 0.853, p = < 0.001) has been observed. This is in agreement with another study that has also established that leptin is involved in development of insulin resistance.[26] Study conducted in 2008, showed a positive correlation with insulin resistance along with elevated leptin levels in obese individuals.[16] Other studies shave also noticed that obesity play a major role in the development of insulin resistance because of the possible role of adipocytokines released from adipose tissue.[28] Cohen et al. studied rat and human hepatoma cell and proved that leptin impairs many signals of insulin.[29] Metabolic syndrome had worse CVD outcome. Though the incidence of CVD and DM is increasing with each day, but these are preventable to a great extent.[30] Studies have shown that weight reduction

not only improves IR, but also has a beneficial role in atherogenic dyslipidemia.[31,32] The effect can be further augmented by use of high-fiber and low-fat diet along with daily exercise.[33] In correlation analysis, discrepancy might be due to small sample size of this study. Moreover, as the patients were not followed so it is not possible to conclude how many people out of total developed diabetes and cardio metabolic complications.

Conclusion

Serum leptin showed a positive correlation with MetS components like waist circumference (WC), waist-hip ratio (WHR), basal metabolic rate (BMI), fasting plasma insulin, insulin resistance (IR) and serum triglyceride (TG), while a negative correlation has been established with plasma high density lipoprotein cholesterol (HDL-c).

Authors Contribution: SM: Design of work, acquisition of data, drafting and final approval. **BRH:** Conception of work, revising and final approval. **MS:** Design of work, interpretation of data, drafting, and final approval. **AA:** Design of work, drafting and final approval.
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