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RESEARCH ARTICLE

Leptin signaling - Leptin resistance in obesity and its correlation with body mass index

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ABSTRACT

Background: Obesity is a worldwide problem and is a risk factor for multiple health problems. Leptin is an adipokine with a role in energy homeostasis and interruption in its action leads to obesity. **Aims and Objectives:** The present study is conducted to determine leptin levels in obese and normal weight adults and correlate the leptin levels with body mass index (BMI) among obese. **Materials and Methods:** The study comprised of 50 healthy obese subjects and 20 normal weight controls in the age group of 30–45 years of either sex. BMI and serum leptin were measured for both subjects and control. **Results:** The study demonstrates higher leptin levels in obese as compared to normal weight adults ($P < 0.0001$) and significant positive Pearson correlation coefficient between serum leptin and BMI among obese. **Conclusion:** Leptin circulates excessively in obese, and measures should be taken to reduce the refractoriness of leptin to regulate the energy homeostasis.

KEY WORDS: Leptin; Obesity; Body Mass Index

INTRODUCTION

Obesity is a worldwide major public health problem and is a nutritional disorder of energy balance characterized by excess accumulation of body fat.[1] The pathogenesis of obesity is multifactorial. Obesity is defined as an increase in the size of fat mass and is associated with grave cardiovascular, neurological, endocrine, and hematological complications. The excessive accumulation of fat in obese is mainly due to interaction between genetic and environmental conditions. Obesity should be closely monitored to avoid future complications and for public health reasons. The most widely used index for measurement of obesity in adults is body mass index (BMI). The BMI is expressed as the ratio of weight in kg and height m^2. The WHO classifies normal weight as BMI 18.5–24.9 kg/m^2 and obesity as BMI >30 kg/m^2.

Body weight is regulated by afferent metabolic and hormonal signals such as insulin, cortisol, cholecystokinin, and leptin informing the brain about the body's energy status. Leptin is a 16 KDa protein hormone of 167 amino acids. It is synthesized, secreted by adipocytes, and is a member of more than 50 identified adipokines that participate in adipose tissue hormone signaling. Leptin acts centrally to decrease appetite and increase energy expenditure. Since the discovery of leptin, its role in pathophysiology of obesity is being studied intensively.

The serum concentration of leptin determines the energy status of the body in adipose tissue. It circulates in the body at a level of 5–15 mg/mL in lean subjects. Its release is increased by overfeeding, insulin, glucocorticoids, endotoxin, and cytokines. Leptin binds to the receptors in hypothalamus, and JAK2/STAT3 signaling mediates the final action of leptin to control feeding energy and storage.

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The leptin-mediated transcriptional proteins stimulate the synthesis of proopiomelanocortin (POMC) which is processed to produce α-melanocyte-stimulating hormone that activates downstream melanocytes 3 and 4 receptors to decrease appetite and increase energy expenditure.

Alteration in JAK2/STAT3 is implicated in impaired post-receptor leptin signaling. Most persons have hyperleptinemia proportionate to Brady fat, yet obese. Limited studies have being conducted to explore the relation of leptin concentration with BMI in local population.

To increase our understanding about leptin concentration in obese and its relation with BMI in local population of Jammu region, the present study was conducted to measure the serum leptin concentrations in obese subjects in a sample of adult population in the region and to compare with those of normal weight subjects. The study also correlated concentration of leptin with BMI in obese subjects.

Aims and Objectives

The study is conducted to determine the leptin concentration in the obese as compared to normal weight subjects and to correlate concentration of leptin in obese with BMI.

MATERIALS AND METHODS

This observational study comprised of 50 healthy obese subjects and 20 normal weight controls in the age group of 30–45 years of either sex. These patients were selected from families, relatives, friends, and colleagues. After obtaining the consent from the subjects and consent from the Ethical Committee, clinical history was taken about diabetes, hypertension, cardiovascular, and pulmonary diseases. Subjects with depression or any acute or chronic disease were excluded from the study.

For BMI, height was measured using wall mounted Stadiometer and weight was determined using weighing balance. BMI was calculated by the formula: BMI = weight in kg ÷ height in m^2. After an overnight fast, blood samples were collected in the morning between 8 and 9 am in plain tubes. The serum was separated and serum leptin was determined using enzyme-linked immunosorbent assay technique.

The data obtained for serum leptin were expressed as mean ± standard deviation both for subjects and controls. The data were analyzed using unpaired *t*-test. A $P < 0.05$ was considered statistically significant. Pearson correlation coefficient was used to analyze the correlation of serum leptin with BMI.

RESULTS

The mean BMI ± standard deviation of cases was 34.50 ± 2.59 kg/m^2 which was significantly ($P < 0.0001$) higher as compared to that of controls 23.06 ± 1.11 kg/m^2. The mean leptin value ± standard deviation of cases was 45.72 ± 3.23 ng/ml which was significantly ($P < 0.0001$) higher as compared to that of controls 7.08 ± 1.34 ng/ml [Table 1].

When BMI was correlated with leptin according to Pearson's coefficient correlation, the relationship was found to be statistically significant ($P = 0.001$) with R value being 0.437 and R^2=0.191 [Figure 1].

DISCUSSION

The present study was conducted to determine leptin levels in obese (with BMI >30 kg/m^2) and normal weight subjects, and also BMI levels were correlated with leptin levels in obese subjects. The study demonstrated higher mean values of leptin in obese as compared to controls, and the relation between the two groups was statistically significant ($P < 0.0001$) [Table 1].

The mean ± standard deviation of BMI in cases was 34.50 ± 2.59 kg/m^2 and in controls was 23.06 ± 1.11 kg/m^2, the relation being statistically significant ($P < 0.0001$) [Table 1]. Our study is in agreement with that of Ali and Abdulmohsen,[2] who measured serum leptin in normal weight and obese men and women of Saudi Arabia. The study demonstrated higher leptin levels in obese than normal weight adults and also higher leptin in obese women as compared to male subjects. Our study is also in agreement with the study conducted by Concidine *et al.,*[3] who demonstrated higher leptin levels in obese subjects. Our study is also in agreement with study conducted by Lee *et al*. [4] who measured leptin levels in obese and average weight adults.

Figure 1 shows Pearson's coefficient correlation between BMI and leptin values in obese subjects. BMI was significantly correlated with the level of leptin with $R = 0.437$ and $P = 0.001$), and the correlation being statistically significant. Our study is in agreement with a study conducted by Kazmi *et al*.[5] who demonstrated a positive correlation between BMI and leptin level in obese.

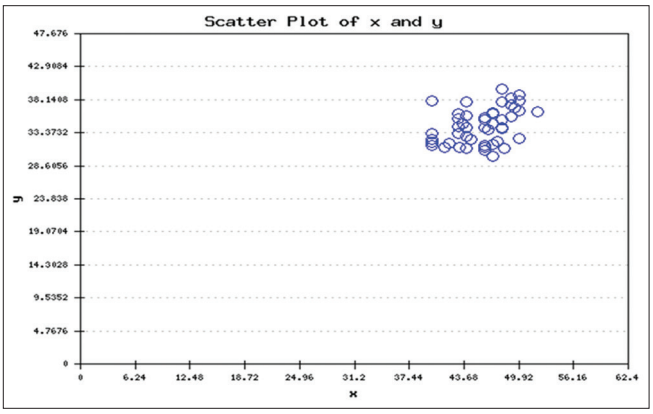

Figure 1: Correlation between body mass index and leptin in obese

Table 1: Comparison of mean BMI (kg/m^2) and mean leptin (ng/ml) values between cases and controls

Variable	Mean±SD		Statistical interpretation (Unpaired *t*-test)
	Cases (*n*=50)	Controls (*n*=20)	
BMI (kg/m^2)	34.50±2.59	23.06±1.11	*t*=19.00; *P*<0.0001; Highly significant
Leptin (ng/ml)	45.72±3.23	7.08±1.34	*t*=51.57; *P*<0.0001; Highly significant

BMI: Body mass index, SD: Standard deviation

The present small sample size observational study demonstrated higher leptin levels in obese as compared to controls. The obese though subjects with higher leptin levels had higher BMI. The obese subjects in the present study had hyperleptenemic proportionate to body fat and appeared to be leptin resistant.

Leptin circulates excessively in obese but is unable to assess the energy status and mediate its action. The resistance of leptin to leptin receptor in hypothalamus hinders the expression of neuropeptides, namely, POMC and melanocyte-stimulating hormone that regulate energy intake and neuroendocrine functions.

The leptin resistance may be due to the high fatty acid levels or mutation in leptin receptor or some abnormality in leptin receptors. The final outcome is disruption of intercellular signaling which mediates the action of leptin. The leptin resistance can be reduced by physical training methods, avoiding high energy junk food and sedentary lifestyles and decreasing the energy intake. Few persons with genetic obesity are leptin-deficient and account for childhood obesity.

Strength

The study confirmed the role of leptin in energy homeostasis.

Limitations

Major limitation was small sample size with no sex-wise distribution of obese subjects, wherein the comparison of their serum leptin levels could be taken up.

CONCLUSION

Leptin is a protective mechanism of the body against energy intake. Leptin communicates to the central nervous system about the abundance of energy stores and restrains food intake to induce energy expenditure. Other than genetic obesity, measures should be taken by the obese to increase the effectiveness of circulating leptin.[5]

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