

# Relationship of Leptin Hormones with Body Mass Index and Waist Circumference in Saudi Female Population of the Makkah Community

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**Abstract:** *Objective:* This study aims to study obesity in Saudi female population represented by Makkah community. *Design:* To study obesity, leptin concentration was measured and other measurements, like body mass index (BMI) and waist circumference (WC) have been used in this study. *Setting:* Departments of Physiology and Biochemistry, Medical College, Umm-Alqura University, Saudi Arabia. *Subjects:* Two-hundred and forty women (n=240) between the ages 18 and 65 participate in this study. Volunteers were divided into three groups. The first group was the normal or control group with (BMI) range from 18 to 29.9, the second group was the obese and characterise with (BMI)  $\geq 30$  and finally obese diabetic group with body mass index (BMI)  $\geq 30$  and suffer from diabetes mellitus. *Main Outcome Measure:* Leptin levels and Anthropometrics measurements. *Results:* Leptin was measured in all the groups and their means found to be (8.4 $\pm$ 1.4) in normal, (56.3 $\pm$ 18.8) in obese and (42 $\pm$ 19.3) in diabetic obese group. Leptin levels were directly associated with BMI in obese and diabetic obese group as follows: ( $r=0.350$ ,  $p=0.001$ ), and ( $r=0.355$ ,  $p=0.001$ ). Also, leptin concentrations were positively correlated with WC in obese and diabetic obese. *Conclusion:* Leptin concentrations were found to be high in both obese and diabetic obese group and showed a directly positive relation with BMI and waist circumference. Understanding that leptin hormone influencing appetite and body weight that cause obesity. However, understanding the relationship of leptin across all obesity categories may help in understanding pathophysiology and perhaps in developing the treatments for obese individuals.

**Keywords:** Obesity, female, leptin, diabetes mellitus, body mass index.

## INTRODUCTION

Obesity is a condition of an abnormal or excessive accumulation of body fat in adipose tissue to the extent that health may be impaired [1]. It is a complex of multifactorial disease that develops from the interaction between genotype and the environment. However, it involves the integration of social, behavioural, cultural, physiological, metabolic, and genetic factors [2]. It is well established that directly or indirectly obesity is associated with various diseases, especially cardiovascular disease, hypertension, diabetes mellitus, sleep apnea, osteoarthritis, fatty liver disease, gallbladder disease, and certain types of cancer. Therefore, its manifestation poses a real threat to health [3].

Saudi Arabia, a Middle Eastern country with a population around 23 million, has undergone significant economic and cultural changes over the past thirty years. Approximately 60% of the population are urbanized and have adopted lifestyle reflecting their diet and physical activity. In Saudi Arabia the prevalence of obesity among female and, to a lesser extent, male adults has reached epidemic proportions. Obesity can be regarded as a major health problem among the Saudi population. A previous study indicated that in the overall population aged 14-70 years, 13.05% of males and 20.26% of females were obese. This value is higher than that reported in the United Kingdom, Australian, Americans and Italian populations [4].

The hypothalamus plays a central role in the regulation of appetite, where the feeding center, located in the lateral hypothalamic nucleus, and the satiety center, located in the ventromedial nucleus, interact. The brain regulates energy homeostasis in response to signals from both adipose tissue and the gastrointestinal tract. The drive to eat and energy expenditure are adjusted so that over time, body weight remains stable [5]. Understanding the physiology of obesity, including the role of appetite as it relates to energy intake and weight gain, is essential for developing efficacious weight-loss therapies. There are also several compounds that appear to participate in the regulation of food intake, including circulating nutrients (e.g., glucose, amino acids, and fatty acids), metabolic compounds (e.g., lactate, pyruvate, and ketone bodies), and hormones (e.g., insulin, glucagon, cholecystokinin, leptin, and ghrelin) [6].

Leptin, (from the Greek word leptos, meaning thin) is a peptide hormone, secreted from adipose tissue, which influences energy homeostasis, immune and neuroendocrine function [7]. In humans, it is well established that plasma leptin levels are directly proportional to percentage body fat. Most obese individuals have high concentrations of leptin in their serum and plasma but exhibit leptin resistance because of decreased leptin transport into the central nervous system or downregulation of leptin receptors [8, 9].

Previous studies have evaluated leptin concentrations in small samples of lean and obese subjects [10]. However, preliminary data available on leptin concentration analysis across the range of BMI, did not use waist circumference (WC). Furthermore, the relationship between leptin level and

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WC have not been assessed in a sample of adults accounting for differences in age, fasting, physical activity and hypertension [11, 12].

The purpose of this study was to evaluate the relationship of leptin with BMI and waist circumference in a random sample of adult women classified as ranging from normal weight to severely obese based on BMI criteria. We anticipated a direct relationship of leptin with BMI and waist circumference.

## MATERIAL AND METHODS

This study was submitted and approved by the University of Umm-Alqura Institutional Review Board, and all subjects signed an informed consent form.

Leptin hormone concentrations were analysed using Human leptin ELISA kit from Linco Research (6 Park Drive, St. Charles, Missouri 63304 USA). The analysis of Leptin was carried out by using DSX Automated ELISA System from (DYNEX Technologies .Inc.).

"BMI and WC" were measured as an anthropometric measurement.

### Subjects

A total of 240 women aged 18-65 participated in this study. They were divided into three groups; (see below). After giving informed consent each participant completed a confidential. The study was carried out at Umm AL-Qura University, AL-Noor Specialist Hospital (Diabetic Centre) and King Abdul-Aziz Hospital (AL-Zaher). All blood analyses were carried out in the University Physiology Department and Professor Sultan research laboratory at Umm AL-Qura University.

**First** - control group (nonobese): 80 volunteers were recruited in this group, which had a BMI ranging from 18 to 29.99.

**Second** - obese group: 80 volunteers were recruited in this group. Their BMIs were  $\geq 30$ .

#### First and Second Groups Met the Following Criteria:

- 1) Not on any diet or use any medication which can interfere with the result.
- 2) Not performing any physical activity, which may interfere with the result.

**Third** - diabetic obese group: 80 volunteers were recruited to this group. Their BMI were  $\geq 30$ .

### Anthropometric Measurements

BMI was calculated as  $\text{kg/m}^2$ . Height was measured using a Harpenden anthropometer (Holtain, Ltd, Crymych, UK) to the nearest centimeter. Weight was measured using a Scale-tronix scale (Sharp Corp, Wheaton, IL, model 695, weighing to 364 kg) to the nearest 0.1 kg. Subjects were divided into five categories of BMI [2]. The categories were as follows: normal weight,  $<25$ ; overweight, 25 to 29.9; obese I, 30 to 34.9; obese II, 35 to 39.9; severely obese,  $>40$ . No subjects had a BMI  $<18.5$ . Waist circumference was

measured by locating the upper hipbone and placing a measuring tape around the abdomen (ensuring that the tape measure is horizontal). It should be comfortable and not cause compression of the skin [13].

### Hormone Levels

Blood samples were collected after an overnight fast. Plasma were obtained by centrifugation of blood samples and stored at  $-70^\circ\text{C}$  at the Microbiology Department.

Following thawing of the samples, leptin levels were measured in duplicate using the human leptin Enzyme Linked Immunosorbent Assay kit. Leptin kits were purchased from the Millipore Corporation Research Inc (StCharles, MO, USA) and were used to test hormone levels at Professor Sultan research laboratory.

### Statistical Analysis

Descriptive statistical analyses were performed using SPSS software (version 11.5, 2002). Pearson correlation coefficients were used to determine the relationship of BMI, waist circumference with leptin concentrations in these subjects groups (nonobese, obese and obese diabetic), while correlation was defined as a measure of the strength of a linear relationship between two variables. The statistical measure of linear association is known as the correlation coefficient, denoted by the symbol  $r$ , and measures how close the points lie to a straight line. Its value always lies between  $-1$  and  $+1$ . The value  $+1$  indicates a perfect positive relationship between the two variables and the value  $-1$  indicates a perfect negative relationship. In addition, p-value is the probability of getting the observed difference, or one even more extreme, in the sample purely by chance from a population, where the true difference is zero. If the p-value is greater than 0.05 then, by convention, we conclude that the observed difference could have occurred by chance and there is no statistically significant evidence (at the 5% level) for a difference between the groups in the population.

## RESULT

The study samples were 240 women between 17 and 65 years old, with a mean age of  $32.7 \pm 13.75$  years, height  $1.54 \pm 6.3\text{m}$ , and weight  $74.9 \pm 17.5\text{kg}$  (See Table 1).

### Leptin Concentration

Mean of leptin concentrations in all three groups were found to be 8.4 ng/ml ( $\pm 1.4$ ) in nonobese, 56.3 ( $\pm 18.8$ ) in obese and 42 ( $\pm 19.3$ ) in the diabetic obese group (See Table 1).

### BMI and Weight

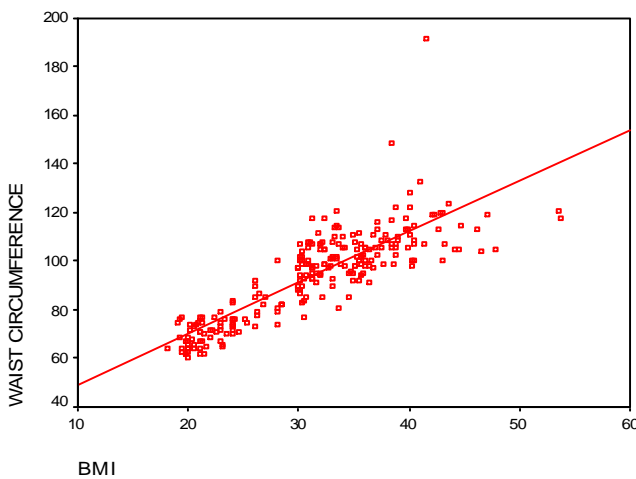
BMI was directly associated with weight and showed a strong positive relation ( $r = 0.935$ ,  $P = 0.000$ ).

### BMI and Waist Circumference

BMI was directly associated with waist circumference and demonstrated a strong positive relation ( $r = 0.840$ ,  $P = 0.000$ ) (See Fig. 1).

**Table 1. Summary of Characteristic Feature of all Volunteers in all Groups such as Age, BMI, WC, Weight, Height and Leptin Concentration**

Character		Normal	Obese	Obese Diabetic	
Age	Range	18-38	18-55	20-58	
BMI		18-29.9	30-53	30-53.6	
WC		60-100	77-149	90-192	
Age (years)	mean±std	20.1±2.3	31.4±12.1	46.6±7.9	
Height (m)		1.55±6.4	1.55±6.4	1.529±6.00	
Weight (Kg)		55.61±7.9	86.5±13.7	82.7±10.2	
BMI		22.7±2.6	35.7±5.2	35.4±4.3	
WC (cm)		72.9±7.5	101.6±12	106.6±12.4	
Leptin Concentration (ng/mL)		8.4±1.4	56.3±18.8	42 ±19.3	
		Max.	10.99	99.60	97.27
		Min.	5.12	8.21	12.71



**Fig. (1).** Correlation between Waist Circumference and BMI.

**Leptin Concentration and BMI in Different Subject Groups**

**In Non-Obese Subjects**

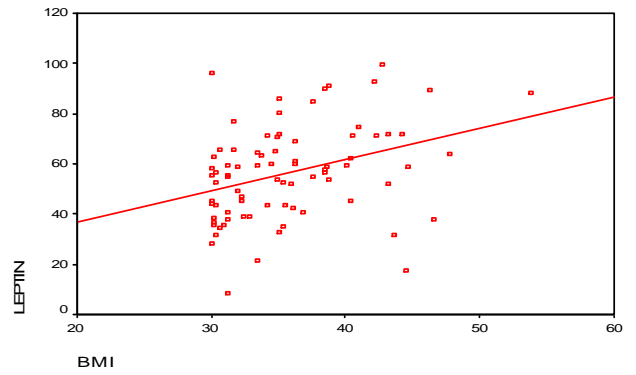
The correlation between leptin concentration and body mass index was linear (data not shown).

**In Obese Subjects**

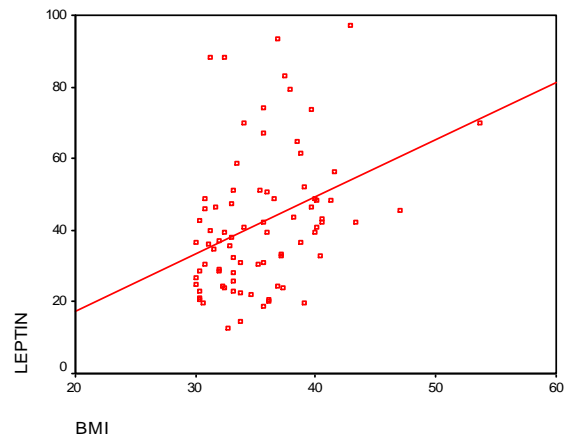
Leptin concentrations were directly associated with Body Mass Index and demonstrate a strong positive relation ( $r = 0.350, p = 0.001$ ) (See Fig. 2).

**In Diabetic Obese Subjects**

Leptin concentrations were directly associated with body mass index and showed strong positive correlation ( $r = 0.355, p = 0.001$ ) (See Fig. 3).



**Fig. (2).** Correlation between leptin concentration and BMI in obese subjects.



**Fig. (3).** Correlation between leptin concentration and BMI in obese diabetic subjects.

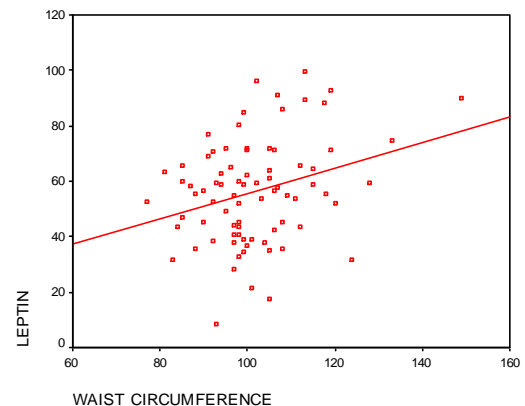
**Leptin Concentration and WC in Different Subject Groups**

**In Non-Obese Subjects**

There was no obvious correlation between leptin concentration and WC ( $r = 0.115, p = 0.310$ ) (data not shown).

**In Obese Subjects**

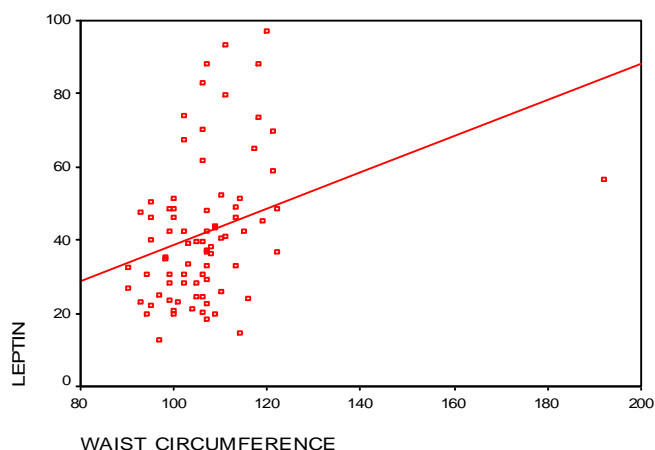
Leptin concentrations were directly associated with WC with a positive correlation ( $r = 0.299, p = 0.007$ ) (See Fig. 4).



**Fig. (4).** Correlation between leptin concentrations with WC in obese subjects.

### In Diabetic Obese Subjects

Leptin concentrations were directly associated with WC and demonstrated a strong positive correlation ( $r = 0.316$ ,  $p = 0.004$ ) (See Fig. 5).



**Fig. (5).** Correlation between leptin concentrations and WC in obese diabetics.

### DISCUSSION

The present work is the first to measure the relation between BMI, WC and leptin concentration to assess obesity in the Saudi female population. Leptin levels were directly associated with BMI and WC, and there were significant positive correlation between leptin and BMI categories.

Obesity is characterised by increased adipose tissue mass which results both from increased fat-cell number (hyperplasia) and increased fat-cell size [14]. Obesity is now extremely common in the world's population, and is replacing under-nutrition and infectious diseases as the most significant contributor to illhealth. Obesity currently affects 30% of the adult population in the United States and 35.5% in KSA [15].

The present study used the body mass index (BMI) and waist circumference (WC) as anthropometric measurement for obesity and fat content. Many studies have confirmed association between BMI and WC, with obesity and fat content. Body Mass Index correlates strongly with measurements of fat mass but it does not distinguish fat mass from lean mass [16]. In contrast, Waist Circumference provides a clinically acceptable measurement for assessing a patient's abdominal fat content [17].

#### Obesity and Leptin Concentration

This study was unique in that leptin concentrations were measured across the BMI rang in adult Saudi women taking into account several risk factors, including waist circumference, age diabetes and physical activity.

Previous studies found that there is little variation in leptin concentrations in the healthy communities according to nationality. A recent study indicated that leptin concen-

trations in Omani control subjects was 10.6 ( $\pm 4.2$ ) ng/ml [18], and in American control subjects leptin concentrations was 7.8 ( $\pm 0.7$ ) ng/ml [19]. In the present study, we found that the normal mean leptin concentration was 8.4 ( $\pm 1.4$ ) ng/ml in Saudi women, which is equivalent to these values.

As previous studies have reported, leptin levels were higher in obese individuals than in normal-weight individuals [20, 21]. Regardless of weight, leptin seems to correlate better with subcutaneous fat rather than with visceral fat in both obese and non-obese subjects [22, 23]. The present study indicates that leptin concentrations were higher in obese subjects (See Table 1). This may be due to a diminished response in the leptin receptor signalling pathway, poor penetration of the blood-brain barrier by leptin, or due to the presence of a less active molecular forms of leptin [24]. In addition, the deficient leptin in nonobese subjects as compared to obese subjects is likely to be a target for leptin therapy, whereas obese subject with high leptin levels is likely to be resistant to leptin therapy [25]. Leptin resistance may occur directly as a result of obesity, but these may also be a lack of sensitivity to circulating leptin which could contribute to the aetiology of obesity [26].

The current study found that serum leptin concentrations were increased in relation to increased body fat content. The positive correlation between body fat and serum leptin is probably explained by the increased release of leptin from large fat cells. Furthermore, leptin can serve as an indicator of fat content and its level may be decreased by reduction of body fat even though BMI values remain unchanged [27].

Previous studies indicate that leptin is directly associated with insulin resistance [28, 29]. Insulin levels were not measured in this study. However, in the diabetic obese group, leptin concentrations were lower than in the obese group but still higher than the normal group, which is in accordance with other studies [30]. This may be due to differences in fat distribution between the obese diabetic and the obese non diabetic group. It has been shown that subcutaneous fat produces more leptin than visceral fat, and diabetics have more visceral fat and less subcutaneous fat. Another possibility is a relative insulin deficiency in the diabetic subjects, because insulin is an important stimulator of leptin production [30].

Uncontrolled diabetes is characterised by behavioural markers and metabolic concerns that arise as a consequence of profound insulin deficiency, including severe hyperglycaemia, depletion of body fat mass, and reduced circulating leptin levels that stimulate food intake [31]. It will be important to know whether the subcellular and tissue distribution of leptin is different in human adipocytes from lean and diabetic obese individuals and whether it can be altered by effectors, such as insulin [32].

There are high levels of leptin in diabetic obesity even although the level of glucose is controlled, because leptin antagonizes the action of insulin in the liver and the results are influenced by the changes in intrahepatic glucose with increased gluconeogenesis and decreased glycogenolysis. It is likely that these metabolic effects of leptin participate in the regulation of hepatic glucose metabolism under physiological conditions [33].

## OBESITY AND ANTHROPOMETRIC MEASUREMENTS

The body mass index (BMI) and waist circumference (WC) are simple and a less time-consuming test to perform in any clinical setting. BMI and WC were found to correlate well with leptin concentration in all subject groups in this study. This is due to the close relation between BMI, WC and body fat content in addition to the responsibility of visceral and subcutaneous fat for producing leptin [34, 35].

In our study, the mean BMI in nonobese, obese and diabetic obese groups were 22.7( $\pm$  2.8), 35.7( $\pm$  5.2) and 35.4( $\pm$  4.3), respectively. BMI increased with increasing weight and the data showed that BMI and leptin concentrations were higher in obese women than in other groups. The means of WC in the nonobese, obese and diabetic obese groups were 72.9( $\pm$  7.5), 101.6 ( $\pm$ 12) and 106.6 ( $\pm$ 12.4), respectively, showing that the high WC was found in the obese and diabetic obese more than in the normal group.

The present study found that there is a positive relationship between BMI and WC, which means that any increase of BMI will be followed by increase in WC and leptin concentration (See Fig. 3).

## CONCLUSION

This study showed a significant linear trend in total leptin, BMI and waist circumference. This study and others indicate that obesity and being overweight are enormous public health problems in Saudi Arabia especially for women.

The high prevalence of obesity among Saudi women could be attributed to limited physical activity as a result of the wide spread use of housemaids, the limited availability of exercise facilities for girls and women in Saudi Arabia and limited awareness in the population of the health risks associated with obesity.

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