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Leptin Level in Obese Diabetic Women in Wad Madani, Sudan

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Abstract: *Obesity is considered a major public health problem associated with changes of leptin as appetite-regulating hormones. High-calorie diet, together with low physical activity has resulted in obesity and diabetes being serious social problems. To evaluate the level of leptin hormone and it is association with obesity, fat distribution and type 2 diabetes (T2D). The study comprised 150 women divided into 3 groups according to BMI value I (normal body weight), II (overweight) and III (obese diabetic). Plasma concentrations of Leptin were determined by sandwich enzyme-linked immunoassay.leptin concentration was found to be significantly higher in group II and III than in group* ***recommendations:*** *Serum leptin levels are higher in the Sudanese obese diabetic group and correlate positively with obesity which seems to be an important link between obesity and T2D. Future studies for illustrating the connection between genetic mutations affecting leptin regulation and obesity is tremendously needed to focus the issue at molecular level and fill gaps regarding obesity thrilling and therapeutics.*

Keywords: Obesity, Diabetes Mellitus Type 2 (T2D), Leptin

Introduction:

Obesity is considered a major public health problem associated with changes of Ghrelin and leptin as appetite-regulating hormones. [1, 2] Currently, Worldwide obesity has nearly tripled since 1975 (WHO, 2017). Nevertheless, overweight and obesity are the fifth leading risk for global deaths. At least 2.8 million adults die each year as a result of being overweight or obese. In addition, 44% of the diabetes burden, 23% of the ischemic heart disease burden and between (7-41) % of certain cancer burdens are attributable to overweight and obesity. [3] Obesity is regarded as one of the main risk factors of T2D development and has been estimated that no less than 90% of (T2D) are overweight or obese. [4]Leptin functions is primarily considered as an anti-obesity hormone and play a wide range of functions in humans such as decreasing appetite and thereby food intake, stimulating and maintaining energy expenditure and acting as a metabolic hormone in a wide range of processes by binding to receptors in the brain[5] as well as with a considerable decrease in levels of the insulin-sensitizing adipocytokines and that is why leptin is known to play an important role in the pathogenesis of obesity.[5] Various adipocytokines may influence insulin sensitivity and therefore may be a link between insulin resistance and obesity. Nonetheless, the recent literature shows that disturbances of adipokines secretion may contribute to peripheral insulin resistance development or impairment of production and action of insulin. [6] Pathophysiological relationships between obesity and (T2D) have not been fully clarified; nevertheless, leptin plays an important role in taking part in the long-term regulation of food intake and causes appetite suppression as well as enhancement of energy expenditure. [6, 7] Moreover, it also decreases lipogenesis and stimulates lipolysis, as well as oxidation of fatty acids and has a direct effect on glucose metabolism. However, chronic hyperleptinemia is thought to impair its physiological function. [8]

Subjects and Methods:

Study subjects and **experimental design:**

A total of 150 women living in Wad-Madani, Sudan with age group ≥18 years were selected to participate in this study and divided into three groups depending on the BMI classification. Anthropometric parameters such as age, height and weight were also measured. WC was measured according to cutoffs reported by WHO (Low risk of disease≤79 cm, increased risk of disease 80-87 cm and substantially increased risk of disease ≥ 88 cm). Body mass indices (BMI) were calculated according to BMI cutoffs proposed by the National Institute of Health (Below 18.5 Underweight, 18.5-24.9 normal weight, 25.0-29.9 overweight, 30.0-34.9 obesity class 1, 35.0-39.9 Obesity class 11 and ≥ 40.0 obesity class 111). [9] Blood samples were collected for hormonal analysis. All subjects were informed about the aim of the experiment and gave written consent for participation in the study. The study protocol was approved by the University of Gezira, Faculty of Medicine (Sudan, acceptance 0254/100/2012).The exclusion criteria were pregnant women, age ≤ 18 years old, chronic medical or psychiatric illness (with exception of obesity related diseases) and user of psychiatric drugs.

Biological material preparation and determination of plasma leptin concentration:

Vein blood samples were drawn from subjects after overnight fasting into heparinized test tubes. Plasma was separated by centrifugation (1000 g, 15 min.), divided into several portions (to avoid thawing-freezing cycles) and kept at –70°C for further examination. In the obtained material, concentrations of selected adipokines - leptin were determined by immunoenzymatic methods using Human Leptin Quantikine ELISA Kit (R&D Systems, USA).

Statistics analysis:

Using SPSS version 16.0 [10]. Descriptive statistics like frequency distributions for categorical variables and the

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means and standard deviations are used to describe the characteristics of the study population. To detect some relationships between variables chi-square tests were adopted to test the significance of these relationships[11]. Correlation coefficients measure the strength and the weakness of the relationships.

Results:

The mean of BMI, age and (WC) of the three study groups are shown in Table (1). However, no, significant correlation between the BMI and the age groups is registered (r=0.00 (*p≤0.05*). Leptin concentration was found to be significantly higher in group II and III than in group I. (p≥0.00 *p*≥0.001 respectively; Table 1). Serum leptin levels are higher in obese diabetic group and correlate positively with obesity, which seems to be an important link between obesity and T2D. The mean leptin level is 23.23±17.79, in normal group; 56.67±16.95 in overweight group and 42.79±24.41 obese diabetic group (Table 1 and Fig. (1&2). Leptin concentration was significantly higher in overweight versus obese diabetic and normal group (P≥0.00) respectively. The comparison of these results revealed statistically significant increase in plasma leptin in overweight versus obese diabetic and normal groups. Table 1 and Fig. 1 and 2 illustrate the correlations coefficient of Leptin level with the BMI and WC in normal, overweight and obese diabetic groups**.** The mean level of Leptin is significantly lower in lean control subjects when compared with overweight subjects while the mean Leptin level is significantly lower in obese diabetic women compared with overweight, but still higher than the level in lean subjects. Fig 2 (A&C) demonstrates the correlation between the leptin hormone, BMI and WC in normal weight and overweight women, while, Fig.2 (B&D) reveals the correlation between leptin, BMI and WC in overweight and obese diabetic group. A highly positive significant correlation between the body (BMI) the WC and plasma leptin levels (r= 0.71 *p≥0.05*) of the participants is verified. Table 1 shows the correlations coefficient of the Leptin hormone with the BMI and WC in the three study groups.

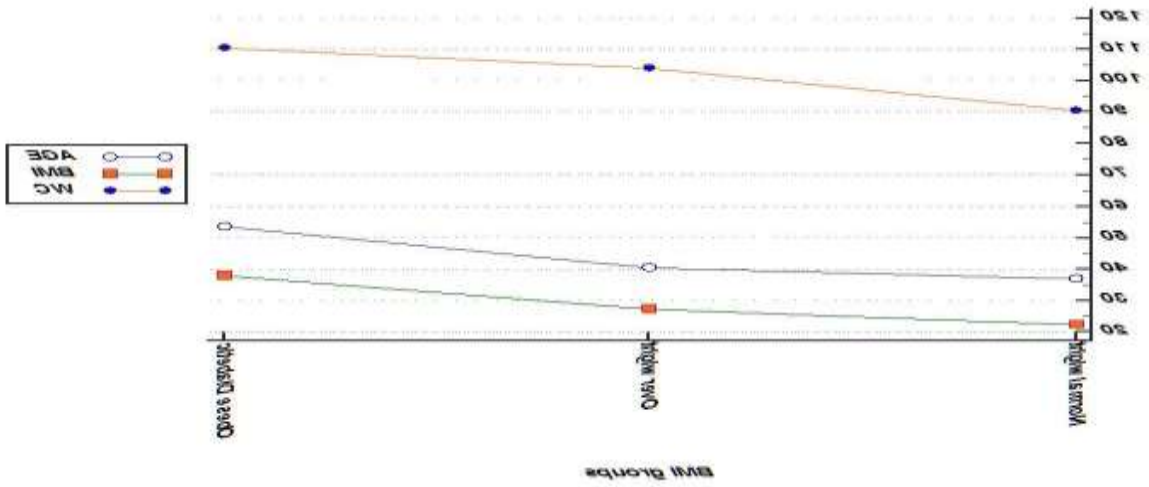

Fig .1: The mean of BMI, age and waist circumference of the three study groups.

Table (1): Comparison of the mean leptin levels in the three study groups (2-tailed Student t-test)

hormone	Categories	Number	Mean ±SD	t-test	P value
Leptin	Normal weight	50	23.23±17.79	1.181	0.00 **
	Overweight	50	56.67±16.95		
	Normal weight	50	23.23±17.79	3.596	0.00 1**
	Obese diabetic	50	42.79±24.41		
	Overweight	50	56.67±16.95	2.741	0.007**
	Obese diabetic	50	42.79±24.41		

Table (2) Correlations of the Leptin of hormone with the BMI and WC in the three study group

Leptin levels		Normal	Overweight	Obese diabetic
BMI	r	-.137	0.050	.147
	p	.342	0.730	0.307
WC	r	0.193	-0.098	-.003
	p	0.179	0.497	-983

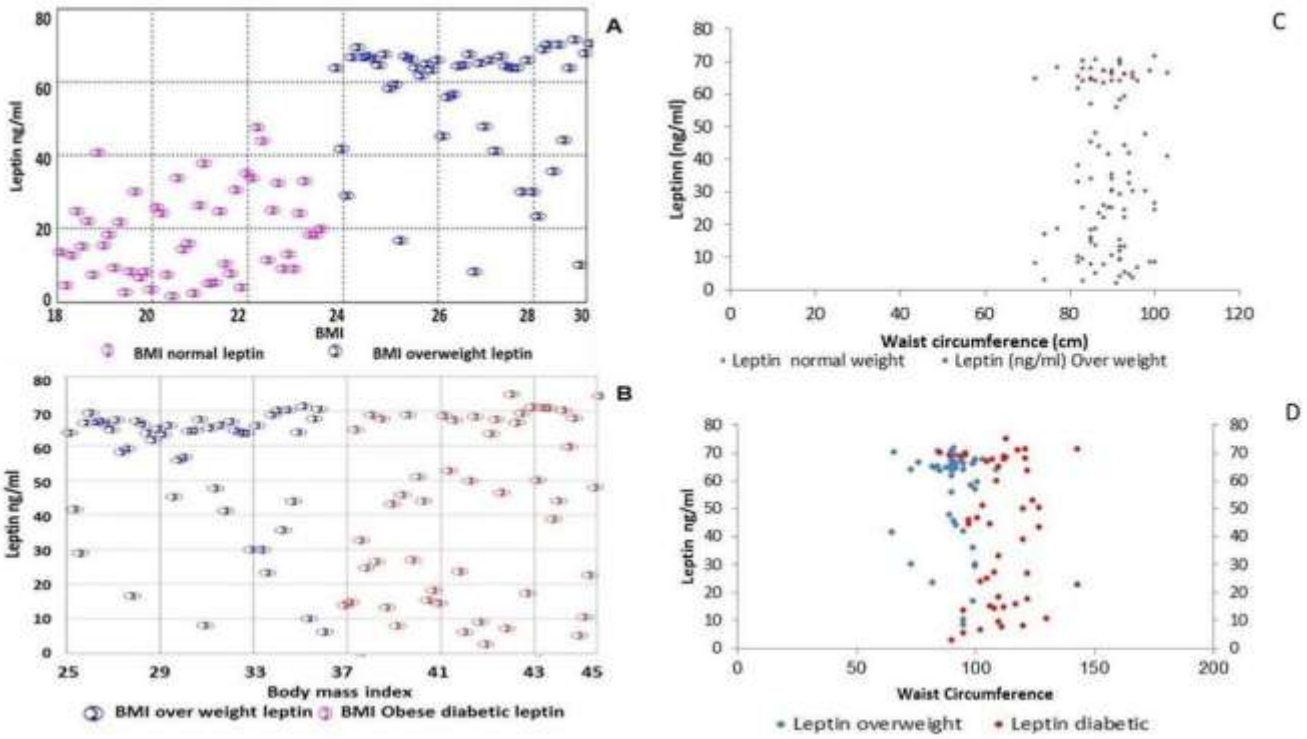

Fig.1: The distribution between leptin hormone, (BMI) and (WC) in the study groups

A: Correlation between the leptin hormone and BMI in normal weight and overweight **B:** Correlation between the leptin hormone and BMI in overweight and obese diabetic **C:** Correlation between the leptin hormone and WC in normal weight and overweight and **D.** Correlation between the leptin hormone and WC in overweight and obese diabetic

Discussion:

Leptin is a hormone secreted by adipose tissue and has established role in maintaining balance between food intake and energy expenditure through its communication with central nervous system.[12] The importance of this study reflects an important attempt to establish a base line data regarding hormonal profile levels in obese diabetic Sudanese women. In the current study, the mean level of Leptin is significantly lower in lean control subjects when compared with overweight subjects, while the mean Leptin level is significantly lower in obese diabetic women compared with overweight, but is still higher than the level in lean subjects. BMI and WC were found to be correlated 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. These results go in consistent with recent study in Korea suggesting that leptin concentrations reflect closely the amount of fat stored in adipose tissues, and plays an important role in energy homeostasis and metabolism.[13] The results of the present study also are consistent with Saudi consequence according to their BMI, average weight and obese. [14] Leptin levels showed a positive correlation with BMI and insulin. [15] Nevertheless, 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. [26] The current study revealed a positive correlation between body fat and serum leptin concentrations. This is probably explained by the increased release of leptin from large fat cells levels. Previous studies showed that leptin is directly associated with insulin resistance [16]. Serum leptin may vary by ethnicity and has been reported as being lower in Sudanese, Bangladeshi and Turkish [17], similar in Chinese [18] but higher in Asian Northern Indian and Saudi subjects with (T2D). Interestingly, the present study reporting lower circulating leptin levels associated with BMI and WC in the obese diabetic subjects. These findings are attributed to the relative insulin deficiency in (T2D) and may probably offer an alternative explanation for the lower leptin levels in diabetic subjects, since insulin is an important stimulator of leptin production and suggests that leptin may be a marker of insulin secretion rather than insulin sensitivity.[19] These results go with many studies that report lower serum leptin in subjects with diabetes in Caucasian and non-Caucasians populations [20], but differ from those reporting similar or higher serum leptin concentrations in subjects with diabetes. [21] In the current study, a linear relationship between serum leptin and (BMI) in women was recorded. A strong significant correlation of leptin with WC is registered. Plasma leptin level was positively correlated with WC and BMI; in overweight subjects in proportion to the degree of adiposity, suggesting that hyperleptinemia may play a role in the pathogenesis of obesity related complications. This correlation may likely suggest its role in the regulation of visceral adiposity .[22] These results are consistent with the results obtained by Wang. [23] However, considerably increased in plasma leptin level was found in overweight as compared to obese diabetic women and normal groups. These results are in consistent with the findings reported by Anusha and Shimizu [24, 25] who reported that, leptin is strongly correlated with adiposity and is a potential determinant of obesity and its complications. Their findings are validated the results and ensure that Leptin together with other adipocytokines affect insulin sensitivity and accepted to play an important role in pathogenesis of obesity-related disorders. The resistance could be due to receptor defects, post receptor defects or disruption of any of the integrative neuronal circuits necessary for leptin action. The physiological interpretation regarding increases of plasma leptin concentrations on overweight and obese with T2D subjects are based on significantly elevated Leptin receptors that are present most abundantly in brain and in various peripheral tissues. Future studies for illustrating the connection between genetic mutations affecting leptin regulation and obesity are needed to focus the issue at molecular level.

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