Gender Differences of Serum Leptin Hormone Levels in Iraqi Population

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ABSTRACT

To evaluate and compare serum Leptin hormone level between Iraqi male & female and the relation between this hormone & BMI in these two groups.

A total of 44 normal male & female subjects were included in this study

{ Group 1 : 22 female } , { Group 2 : 22 male }.

Serum Leptin hormone, BMI &fasting blood glucose were measured for both groups.

Serum Leptin level in group 1 was $(8.82 + 2.9 \ \mu g/L)$ where as in group 2 it was $(4.65 + 3.2 \ \mu g/L)$. These changes were statistically significant. Fasting blood glucose levels were technically within the normal value $(116.43 \pm 3.4 \ mg/dl)$ for group 1 & $(118.52 \pm 2.9 \ mg/dl)$ for group 2. BMI levels were comparable in both groups during the study, with slight elevation in group 1 [$24 \pm 1.73 \ kg/m^2$ for group 1 & $23 + 1.98 \ kg/m^2$ for group 2] which within the acceptable limit as far as safety concern.

Leptin, an adipocyte-derived hormone known to play an important role in body-weight regulation, the result of this study shows that Leptin is presented differentially in Iraqi men and women; in which it is significantly higher in women than in men serum . These observations are potentially important for the understanding of differences between men and women in regulation of food intake, weight gain, and body fat distribution. The relation between Leptin & the BMI in male and female in this study may open another approach for this hormone to be involved in –fertility & in pubertal development.

الخلاصة

لغرض قياس ومقارنة هرمون اللبتين (Leptin) بين الذكور والإناث في العراق وعلاقة مستوى الهرمون المذكور مع نسبة كتلة الجسم BMI في كلا الجنسين .

شملت الدراسة 44 شخص ، تم تقسيمهم إلى مجموعتين : الأولى ضمت 22 أنثى والمجموعة الثانية تضمنت 22 ذكرا . تم قياس مستوى هرمون اللبتين ونسبة كثلة الجسم ومستوى سكر الدم في حالة الصيام لكلا المجوعتين . أظهرت نتائج قياس الهرمون في المجموعة الأولى 28.8 \pm 2.0 مليكر و غرام /لتر . في حين كان مستوى الهرمون في المجموعة الثانية \pm 4.65 مليكر و غرام /لتر ، في حين كان مستوى الهرمون في المجموعة الثانية \pm 3.2 مليكر و غرام / 116.40 لنر ، حيث أن الفرق كان معنويا بصورة واضحة . وكان مستوى سكر الدم ضمن القيم الطبيعية : 16.43 \pm 3.2 ملغرام /100 مل المجموعة الثانية . وكانت نسبة كثلة الجسم متقاربة بين المجموعتين مع وجود ارتفاع قليل في المجموعة الأولى و 1.73 \pm 3.4 كغم /م² مقابل 2.5 كغم /م² مقابل 2.5 كغم /م² المجموعة الثانية) و هي ضمن المستويات الطبيعة

ان اللبتين و هو هر مون مشتق من الخلايا الدهنية ليقوم بتنظيم وزن الحسم. لقد اظهرت نتائج هذه الدراسة ان مستوى هرمون اللبتين يظهر فروقا واضحة بين الرجال والنساء العراقيين ، حيث ان مستوياته اعلى في النساء مما هو في الرجال والنساء العراقيين ، حيث ان مستوياته اعلى في النساء مما هو في الرجال والنساء في تنظيم تقيل الطعام وزيادة الوزن وتوزيع الدهون في الجسم . ان العلاقة بين مستوى الهر مون ونسبة كتلة الجسم في كل من الرجال والنساء في هذه الدراسة قد يمهد لدراسة علاقة مستوى هذا الهرمون مع درجة خصوبة وتطور البلوغ في كلا الجنسين .

INTRODUCTION

Leptin is a recently discovered hormone¹ that is mainly synthesized by adipose cells and secreted into the bloods tream in amounts relative to the quantity of body fat. Plasma leptin levels in humans are strongly correlated with body mass index (BMI) and total fat mass (Figure 1) and are elevated in obese subjects.²

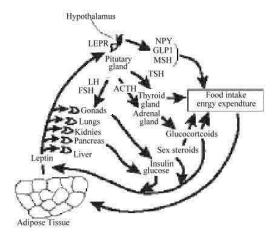


Fig.1. Schematic representation of central and peripheral actions of leptin on bodyweight regulation and on metabolic and endocrine parameters LEPR = leptin receptor; NPY = neuropeptide Y; GLP -1= glucagon-like peptide-1; **MSH** melanocyte-stimulating hormone; LH = lute iniz ing hormone; FSH =folliclestimulating hormone; **ACTH** adrenocorticotropic hormone; TSH thyroid-stimulating hormone. Adapted and updated from Scott J. New chapter for the fat controller.

Leptin is thought to have an "adipostat" function;that is, it acts as a signal informing the brain about the amount of fat stored in the body, through which the brain can regulate energy intake and energy expenditure in order to keep body weight constant (Figure 1). Therefore, when leptin levels are low, appetite will be stimulated with limited use of energy, and when leptin levels are high, appetite is reduced and energy use is stimulated.

In rodent experiments, leptin administration leads to weight loss through

reduction in food intake and increased energy expenditure.⁵ In humans, however, leptin levels are very high in obese people, which suggests the existence of a leptin – resistance state, analogous to insulin-resistance in type 2 diabetes,⁴ the exact mechanisms for this resistance are not clear yet.

The leptin receptors in brain is mainly present in the hypothalamus and choroid plexus, where food intake is regulated through the modulation of several neurotransmitter pathways, such as neuropeptide -Y, glucagon-like peptide-1, and melanocyte-stimulating hormone pathways. Leptin may also modulate pituitary secretion of thyroid-stimulating hormone, adrenocorticotropic hormone, and gonadotropins, thus influencing indirectly the secretion of triiodothyronine / thyroxine, cortisol, and sex hormones, respectively, all of which have effects on energy balance 7.

MATERIALS and METHODS:

Forty four apparently healthy male & female (age between 23 and 35 years) were included in this study and consedered as two groups to determine serum leptin concentration, BMI and fasting blood glucose for each individual.

EXCLUSION CRITERIA:

Any individual that has hyperglycemia or BMI > 25 was excluded from this study.

METHODS

Venous blood samples (6 ml) were taken from each subject to mesure serum leptin and fasting blood glucose levels. The sample was transferred into a clean plain tube, left at room temperature for 30 minutes for clotting, centrifuged, and then the serum from all blood samples was separated and stored at $-20\,\mathrm{C}$ for subsequent study .

Determination of fasting blood glucose:

Enzymatic & colorimetric method (Glucose oxidase GOD/ Peroxidase POD) , the principle of this method depends on enzymatic determination of glucose according to the following reaction⁹:

Determination of serum Leptin (ELISA):

Enzyme immunoassay (microtiter strips) for the quantitative determination of Leptin in human serum. ¹⁰

STATISTICAL ANALYSIS:

Measurement of variables done by using numbers, percentage, means +/- standard deviation. Differences between variables were measured by using ANOVA test when it needed.

RESULT

The studied variables are listed in table 1. Serum leptin hormone levels are presented in table 2 (8.82 + 2.9 $\mu g/L)$ in group 1 & (4.65 + 3.2 $\mu g/L)$ in group 2,The variation between the two groups was statistically significant (P < 0.05) . Gender differences between the two groups in serum Leptin shown clearly in Figure 2,while fig 3 shows the difference in serum leptin levels between Iraqi women and the reference values for femal subjects.

Table (1) The studied variables are listed

Variables	Group -1- (n=22)female	Group –2- (n=22)male
Age (years)	27.4 ± 4.18	30 56 ± 3.26
BMI (K g/m ²)	24 ± 1.73	23 ± 1.98
Fasting b bod glucose (mg /dl)	116.43 ± 3.4	118.52 ± 2.9

Table (2)Serum leptin hormone levels are presented in table 2

	Group -1- (n=22)female	Group –2- (n=22)male
Leptin hormone (µg/L)	8.82 ± 2.9	4.65 ± 3.2
Reference Value	7.4 <u>+</u> 3.2	3.9 <u>+</u> 2.8

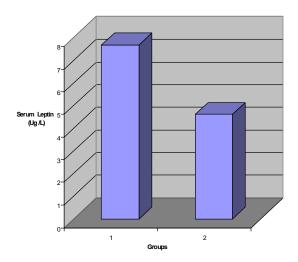


Fig 2: Gender differences in Leptin level between the two groups

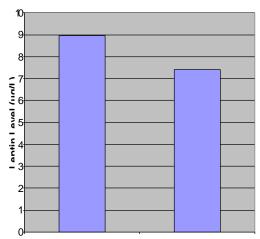


Fig 3: Comparison between Iraqi (1) and other normal female (2) in Leptin levels

DISCUSSION:

This study is one of the newest studies that discuss the variation in one of the newly discovered hormones (Leptin) between male & female subjects in Iraq. The knowledge of this relation is very important to understand various problems associated with obesity, puberty & infertility.

From the results (table 2 &fig 2)of this study serum Leptin levels are significantly higher in women than in men (p< 0.05). This study which is done in Iraq to evaluate the values of leptin hormone in normal male & female subjects to be compared with the study of Reitman & coworkers the results shows a higher values in Iraqi female (Mean =8.82 ug/L) than other female values (mean = 7.4

ug/L) ³; These differences may be due to the fact that Iraqi women have higher fat mass than the other women. A comparable results was found in male with different studies.

At first, such differences between Iraqi male & female subjects were thought to reflect the differences in body composition between men and women. Women in general have a higher percentage of fat mass for the same body weight or BMI. Since leptin reflects mainly the amount of body fat, this seemed to be a logical explanation for the observed gender differences¹¹. However, the se gender differences and their relationship to body composition were examined ,and leptin levels were found to be significantly higher in women with comparable BMI or fat mass.

A second explanation was thought in the differences in fat distribution between men and women. Women generally have more peripheral fat accumulation (especially at the level of the hips), whereas obese men have more abdominal (especially visceral) fat. It was shown in several in vitro studies that subcutaneous adipocytes produce more leptin than fat cells derived from the omental fat depot; this is especially true in women. 12,13 In vivo studies also showed that leptin levels had a stronger association with peripheral¹⁴ or subcutaneous fat than with intra- abdominal or visceral fat, as measured by computed tomography scan. 15 Thus, the fact that women have more subcutaneous fat, which secretes more leptin, seems an additional reason for the higher leptin levels in women. However, even after correcting for the amount of subcutaneous fat, leptin levels are still found to be significantly higher in women.¹⁰

CONCLUSION

The results of this study are potentially important for the understanding of differences between men and women in regulation of food intake, weight gain, and body fat distribution; but since these differences in body composition between men and women may not be the only reason to explain the differences in leptin levels completely, other factors must play a role, like Steroid hormones but the exact mechanism or interaction is not yet known. These findings seem to indicate that this recently discovered hormone may play a role obesity, infertility & other disease states.

REFERENCES

- 1. Zhang Y, Proenca R, Maffei M, et al, Positional cloning of the mouse obese gene and its human homologue. Nature; . 1994 372,425-431.
- 2. Maffei M, Halaas J, Ravussin E, et al. Leptin levels in human and rodent: Measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nat Med; 1995,1,1155-1161.
- 3. Reitman M ,Gavrilova O Leptin & its role in pregnancy and fetal development,Biochemical Society Transaction ,2001,29,68-72,6.
- **4.** Ostlund RE, Yang JW, Klein S, Gingerich R. (Relation between plasma leptin concentration and body fat, gender, diet, age, and metabolic covariates. J Clin Endocrinol Metab, 1996,81,3909-3913.
- 5. Halaas J, Gajiwala K, Maffei M, et al. ,Weight-reducing effects of the plasma protein encoded by the obese gene. Science; 1995,269,543-546.
- **6.** Tartaglia LA, Dembski M, Weng X, et al Identification and expression cloning of a leptin receptor, OB-R. Cell 1995,83:1263-1271.
- 7. Wauters M, MSc, and Luc Van Gaal, MD, PhD. Gender Differences in Leptin Levels and Physiology: A Role for Leptin in Human Reproduction ;The Journal of Gender Specific Medicine, 1999, 2[5],46-51.
 - **8.** Ronald C.K. New hormones offer understanding & promising treatment for diabetes & obesity.International journal of obesity advanced online publication, 2004,14,10: 1-12
 - **9.** Syrbio diagnostic reagents for laboratories under license of EUROBIO laboratories –Paris 2002.
 - 10. Considine R.V., Sinha M.K.; Serum immunoreactive Leptin Concentrations in normal weight and obese humans, the new England Journal of Medicine, 1996, 123,23.
 - 11. Wauters M, Mertens I, Considine R, et al. Are leptin levels dependent on body fat distribution in obese men and women? Journal of Eating and Weight Disorders; 1998,3,124-130.
 - 12. Couillard C, Mauriege P, Prud'homme D, et al. Plasma leptin concentrations: Gender differences and associations with metabolic risk

factors for cardiovascular disease. Diabetologia; 1997,40,1178-1184.

- **13**. Van Harmelen V, Reynisdottir S, Eriksson P, et al. Leptin secretion from subcutaneous and visceral adipose tissue in women. Diabetes; 1998,47,913-917.
- 14. Niskanen LK , Haffner S , Karhunen LJ
- et al. Serum leptin in obesity is related to gender and body fat topography but does not predict successful weight loss. Eur J Endocrinol; 1997,137:61-67.
- 15. Vettor R , Vicennati V, Gambineri A , et al.,Leptin and the hypothalamic-pituitary-adrenal axis activity in women with different obesity phenotypes. Int J Obesity Relat Metab Disord 1997,21,708-711.