

**Leptin Level in Newly Diagnosed Iraqi Acromegaly Patients****Noor ThairTahir***National Diabetic Center**noor9t@yahoo.com***Abstract:**

Acromegaly is a serious endocrine disease resulting from an increase of growth hormone in the blood. Excessive growth hormone secretion may be caused by an adenoma of the pituitary. This study was designed to assess the effect of serum leptin concentration on acromegaly patients with both gender and its relation with some biochemical analysis. The study conducted 96 subjects (48 acromegaly patients and 48 controls) aged between (30-70) years who were attending the National Diabetic Center/ Al-Mustansirya University and Al-Yarmuk Teaching Hospital. Fasting blood sugar, lipid profile, growth hormone, insulin like growth factor-1, and serum leptin concentrations were measured for each individual. The results explained a significant increased in body mass index, triacylglycerol and low density lipoprotein cholesterol, ( $P<0.05$ ) in acromegaly patients when compared with control group. Fasting blood sugar, serum growth hormone and serum insulin like growth factor-1 concentrations explained a highly significant increased, ( $P<0.01$ ). While serum leptin concentration was significantly decreased. Fasting blood sugar, triacylglycerol, low density lipoprotein, serum growth hormone, serum insulin like growth factor-1, and serum leptin concentrations showed a significant increased in female patients when compared with male acromegaly patients, ( $P<0.05$ ). This study showed that higher serum leptin levels with higher concentrations of triacylglycerol and low density lipoprotein cholesterol might play a vital function in the progress of acromegaly disease. Also, high serum leptin levels observed in female acromegaly patients when compared with male acromegaly patients, the present study suggested the role of leptin hormone as one of the biomarkers affecting in acromegaly patients..

**Key words:** Acromegaly, growth hormone, insulin like growth factor-1, leptin, lipid profile.

**الخلاصة:**

مرض تضخم الأطراف هو احد أمراض الغدد الصماء الخطيرة ينتج من زيادة هرمون النمو في الدم. زيادة إفراز هرمون النمو من الغدة النخامية نتيجة حدوث ورم في الغدة النخامية. صممت هذه الدراسة لتقييم تأثير تركيز اللبتين لدى مرضي تضخم الأطراف في كلا الجنسين وعلاقته مع بعض المتغيرات الكيموحيوية. تضمنت الدراسة 96 شخصاً (48 مريضاً مصاباً بتضخم الأطراف و48 من الأصحاء) تراوحت أعمارهم بين 30-70 سنة من المراجعين للمركز الوطني للسكري ومستشفى اليرموك التعليمي. تم قياس تركيز سكر دم الصائم، الدهون، هرمون النمو، عامل النمو الشبيه بالانسولين-1 وهرمون اللبتين. أظهرت النتائج زيادة معنوية في معدل كتلة الجسم، الدهون الثلاثية، البروتينات الدهنية واطئة الكثافة ( $P<0.05$ ) لدى المرضى المصابين بتضخم الأطراف عند مقارنتهم بمجموعة الأصحاء. كما وجدت زيادة معنوية مرتفعة لسكر دم الصائم، تركيز هرمون النمو، تركيز عامل النمو الشبيه بالانسولين ( $P<0.01$ ) بينما أظهر تركيز هرمون اللبتين انخفاضاً معنوياً. كما أظهر سكر دم الصائم، الدهون الثلاثية، البروتينات الدهنية واطئة الكثافة، هرمون النمو، عامل النمو الشبيه بالانسولين-1، وهرمون اللبتين زيادة معنوية لدى النساء المصابات بتضخم الأطراف مقارنة بالرجال المصابين بتضخم الأطراف. أظهرت هذه الدراسة أن ارتفاع تركيز هرمون اللبتين في الدم مع وجود تركيز عالي من الدهون الثلاثية والبروتينات الدهنية واطئة الكثافة قد تلعب دوراً هاماً في تطور مرض تضخم الأطراف. أيضاً، لوحظ ارتفاع مستويات هرمون اللبتين في مصل النساء المصابات بتضخم الأطراف عند مقارنتهم بالرجال من نفس المرض في هذه الدراسة حيث يبرز دور هذا الهرمون كاحد العوامل البايولوجية المؤثرة على مرضي تضخم الأطراف.

**كلمات مفتاحية:** مرض تضخم الأطراف، اللبتين، هرمون النمو، عامل النمو الشبيه بالانسولين-1، صورة الدهون.

## Introduction:

Acromegaly is infrequent disease and uncommon disorder manifested by an excess of growth hormone (GH) secretion<sup>(1)</sup>. the occurrence of 40 to 70 cases per million people and an annual prevalence of 3 to 4 new cases per million<sup>(1,2)</sup>. It is manifested by gradually progressive acquired somatic defects chiefly including the face and extremities and systemic manifestations of elevated serum growth hormone (GH) concentration and insulin like growth factor (IGF-1) concentration<sup>(3)</sup>. Major manifest alterations in untreated patients are extension of the hands, the feet, the brow and the nose are enlarged, the jaw and zygomatic arches are prominent<sup>(4)</sup>. The hypersecretion nearly all cases led to a pituitary somatotrophic adenoma<sup>(5)</sup>. Usually, the diagnostic of acromegaly patients is delayed for years<sup>(6)</sup>. Excessive GH and IGF-1 secretion may cause metabolic and soft tissue, changes organ enlargement and bone growth and responsible for the growth of almost all tissue and cells, its ensuing adenoma in pituitary<sup>(7)</sup>.

Leptin is a 16 KD protein hormone that participate as a key function in regulation of energy expenditure and energy intake, counting appetite control and metabolism in the circulation in amounts proportional to body fat<sup>(8)</sup>. Leptin level is likely to vary under a variety of nutritional, physiological and disease situations<sup>(9)</sup>. Growth hormone acts on adipose tissue and its harmful consequence on glucose metabolism and insulin signaling<sup>(10)</sup>. The mechanism by which leptin and GH are inversely associated has not been assessed. Leptin may reduce GH secretion or GH may reduce leptin secretion and numerous regression analysis confirmed that serum leptin levels were also inversely related with IGF-1<sup>(11)</sup>.

This study was designed to assess the effect of serum leptin concentration among acromegaly patients with both gender and its relation with some biochemical analysis.

## Materials and Methods:

This study included 96 subjects (48 acromegaly patients and 48 healthy controls); their ages between (30-70) years who were attending the National Diabetic Center/ Al-Mustansirya University and Al-Yarmuk Teaching Hospital, during the period from January 2014 until the end of December 2016. Serum sample was collected for basal measurements of GH, IGF-1, and leptin in 48 acromegaly patients (24 male and 24 female). All information were obtained directly by medical history was taken by a specialized physician. Fasting blood sugar (FBS), lipid profile {total cholesterol (TC), triacylglycerol (TAG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C)} were estimated using Randox Diagnostic kit.

Leptin hormone levels were estimated by the DRG leptin ELISA kit<sup>(12)</sup>. Growth hormone levels were determined by (IRMA- Immunotech, France)<sup>(13)</sup>, and IGF-1 levels were estimated by (IRMA- Immunotech, France)<sup>(14)</sup> (details are found in appendix).

All subjects were untreated and they did not hold any surgical procedure for acromegaly patients.

The statistical analysis and registrations of data were carried out by using Microsoft Office Excel 2010 Worksheet. Differences considered of statistical significance according to the t-test at P-value < 0.05 and < 0.01.

## Result:

Body mass index (BMI), TAG and LDL-C levels showed a significant increase in acromegaly patients when compared with control group, (P < 0.05). Also FBS, serum GH, and IGF-1 concentrations explained a highly significant increase in acromegaly patients as compared to the control group, (P < 0.01). While serum leptin concentration was significantly decreased in acromegaly patients as compared to the

control group, table (1). Table (2) showed descriptive parameters between male and female acromegaly patients. Serum FBS, TAG, LDL-C, GH, IGF-1, and serum

leptin concentrations showed a significant increase in female patients when compared with male acromegaly patients, ( $P < 0.05$ ).

**Table (1): Characteristics parameters between acromegaly and control groups**

Parameters	Acromegaly (n=48)	Control (n=48)
	(means±SD)	(means±SD)
Age (years)	45.59±10.04	43.86±4.52
BMI (Kg/m <sup>2</sup> )	32.12±6.8*	25.01±3.40
FBS (mmol/l)	9.38±1.60**	4.30±1.25
TC (mmol/l)	6.52±0.32	6.21±0.35
TAG (mmol/l)	3.34±0.91*	2.41±0.16
HDL-C (mmol/l)	1.32±0.15	1.83±0.42
LDL-C (mmol/l)	4.32±1.58*	2.58±1.70
GH (ng/ml)	9.03±2.31**	1.43±0.14
IGF-1 (ng/ml)	1123.74±56.18**	242.20±21.03
Leptin (ng/ml)	18.11±3.31**	24.82±2.22

\* Significant  $< 0.05$

\*\* Highly significant  $< 0.01$

**Table (2): Descriptive parameters between**

Parameters	Acromegaly	
	Male (n=24)	Female (n=24)
	(means±SD)	(means±SD)
Age (years)	47.51±11.60	47.62±8.90
Age of onset (years)	38.70 ± 8.80	34.33 ± 3.40
BMI (Kg/m <sup>2</sup> )	34.25 ± 4.20	33.12 ± 3.80
FBS (mmol/l)	6.21±1.50*	8.33±1.40
TC (mmol/l)	6.23 ± 0.50	6.10 ± 0.60
TAG (mmol/l)	2.01 ± 0.40*	2.41 ± 0.90
HDL-C (mmol/l)	1.41 ± 0.20	1.80 ± 0.70
LDL-C (mmol/l)	3.00 ± 0.70*	4.52 ± 0.90
GH (ng/ml)	9.79±1.30*	10.24±3.90
IGF-1 (ng/ml)	605.23±24.10*	772.51±41.70
Leptin (ng/ml)	9.81±2.60*	13.02±4.40

\* Significant  $< 0.05$

**Discussion:**

Acromegaly is frequently the consequence of GH secretion foremost to anatomical change and metabolic dysfunction due to high levels of GH and IGF-1<sup>[15]</sup>. In healthy subjects, GH secretion is under the double regulation of somatostatin and GH-releasing hormone (GHRH) with differences in the secretion of somatostatin mortal the primary model of regulation<sup>[16]</sup>. This study showed a highly significant increased of GH and IGF-1 in acromegaly patients as compared to the control group, this is in agreement with results of other studies<sup>[16,17]</sup>. Also, there was a highly significant raise of FBS in acromegaly patients when compared to the control group, these results agreed with the those of Mohammad et al., (2013). Elevation of GH levels cause increased hepatic glucose production and faulty utilization of glucose at peripheral tissues causing stimulation of insulin release. Growth hormone play an important role in lipid metabolism; the result has found an increased of TAG and LDL-C levels in acromegaly patients when compared with control group<sup>[18]</sup>. Dyslipidemia is one of the frequent complications in newly diagnosed acromegaly having high level of GH<sup>[19]</sup>. Increased FBS cause insulin resistance, reduced insulin action that cause increase lipolysis as the insulin is effective inhibitor of lipolysis<sup>[20]</sup>. Growth hormone leads to increase TAG levels and due to decreased in hepatic lipase activity caused by direct achieve of GH on TAG metabolism<sup>[21]</sup>. Serum leptin level showed significant decrease in acromegaly patients as compared to the control group, this is in agreement with previous studies<sup>[22,23]</sup>. That stated decreased leptin level in acromegaly patients as compared to the control group.

Serum levels of FBS, GH, IGF-1 were increased in female acromegaly patients as compared with male acromegaly patients, this is in agreement with Svetozaret al., (2000)<sup>[24]</sup>. Excess GH and insulin increase free fatty acid and ketone body production

via stimulation of lipolysis and these effects might have been due to impairment of insulin sensitivity.

The present study assessed the association between leptin levels and some risk factors of coronary artery diseases like TAG and LDL-C and demonstrated that serum leptin concentrations differe between male and female acromegaly patients, Serum leptin level significantly increased in female acromegaly patients when compared with male acromegaly patients, this is in agreement with Akram et al., (2011)<sup>[25]</sup>, suggesting that acromegaly patients have increased lean body mass and decreased percentage of body fat<sup>[26]</sup>.

High serum leptin levels seen in female patients in the current study were consistent with earlier studies<sup>[27,28]</sup>, suggesting the role of this hormone as a mediator in human atherosclerosis.

Sattar et al., established a significant positive relationship between serum leptin and TAG and TC levels<sup>[29]</sup>. The inconsistencies between the findings of the present study and other studies may be explained by the study design and sample size. However, this is the first study with patients having acromegaly in Iraqi population. Still the findings of current study are preliminary and further studies should be carried out to confirm the results.

**Conclusions:**

This study showed a higher serum leptin levels with higher concentrations of TAG and LDL-C might play a vital function in the progress of acromegaly disease. Also, a higher serum leptin levels observed in female patients revealed a high body fat. So, it was suggesting role of this hormone as one of the biomarkers affecting in acromegaly patients.

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