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## Determination of the Level of some Adipokines in Hypo-and Hyperthyroids Patients in Baghdad City

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#### Abstract:

Determination of the level of adipokines (obestatin, vaspin, tumor necrosis factor- $\alpha$  and interleukin-6)in hypo-and hyperthyroid patients from Educational Baghdad Hospital in Baghdad City was investigated. Fifty patients with hypothyroidism and Fifty patients with hyperthyroidism were selected. A control group of thirty euthyroid persons was included. Blood was collected by vein puncture and serum was separated and stored at -20C. Adipokines (obestatin, vaspin, tumor necrosis factor- $\alpha$  and interleukin-6) were estimated using ELISA method. The findings show a significant (p<0.05) increase in obestatin level in hypothyroid patients, while there is no significant difference in hyperthyroid patients compared with the euthyroid subjects. In addition, this study demonstrated a significant (p<0.05) increase in vaspin means in hypothyroid patients compared with euthyroid group. In hyperthyroid patients, there is a significant (p<0.05) decrease in vaspin level in comparison with euthyroid subjects. Furthermore, there is a significant (p<0.05) increase in tumor necrosis factor- $\alpha$  level in hypothyroid and hyperthyroid patients as compared with the euthyroid subjects. The results of this study also explain a significant (p<0.05) increase in interleukin-6 level in hyperthyroid patients, while there is non-significant difference in hypothyroid patients compared with the euthyroid subjects.

It is concluded from this study that the levels of interleukin-6 and tumor necrosis factor-  $\alpha$  increased in hyperthyroidism and decreased in hypothyroidism. Obestatin and vaspin were increased significantly in hypothyroid patients.

Keywords: Obestatin, vaspin, tumor necrosis factor- $\alpha$ , interleukin-6, hyperthyroid.

### Introduction:

Adipose tissue has many functions such as energy storage, secreting a group of chemicals as hormones; growth factors and cytokines[1, 2]. This tissue is grouped into brown and white tissue[2, 3].

One of the recently recognized adipokines secreted from the white adipose tissue (WAT); vaspin, with insulin-sensitizing influences [1, 3]. Vaspin concentrations are elevated significantly in type 2diabetes mellitus [2]. Uncontrolled diabetes and weight decrease have cancelled vaspin expression [4]. Interleukin-6 (IL-6) is cytokine secreted by many cell kinds including macrophages, T and B lymphocytes, fibroblasts, endothelial cells, and cancer cells [5, 6]. IL-6 has been known to exert different biologic activities on many types of target cells [5]. It has an important role in the regulation of inflammatory process, immune responses and growth as well as development of thyroid cells [6, 7, 8].

Tumor necrosis factor- $\alpha$  was (TNF- $\alpha$ ) produced by special cells during immune responses playsa vital role inflammatory and immunity responses[5]. It has been found that inflammatory cells secrete a great proportion of tumor necrosis factor in thyroid tissue[6].

Obestatin is a gastrointestinal-peptide hormone[9]. Its expression occurs in the thyroid gland, pancreas and intestine[10]. The role of this peptide is still controversial. Investigations show its action (related glucose and lipid metabolism, body weight and energy homeostasis) conflict to those that reveal no biological function of obestatin. These adipokines secreted by follicles in thyroid gland might have an effect on the autoimmunity (self-immune diseases) as rare and few studies concerning the [5] association between these adipokines and thyroid diseases [11, 2, 9]. This study was conducted to determine the levels of the above- mentioned adipokines in hypo-and hyperthyroid patients in Baghdad City.

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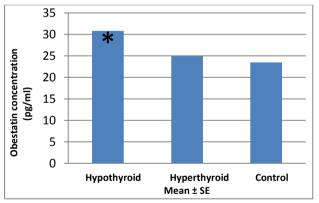
#### **Material and Methods:**

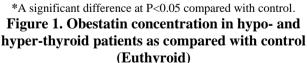
Fifty patients with hypothyroidism and fifty with hyperthyroidism were choosen. Thyroid disorders were determined by endocrinologist. The time of sample collection was during a two-month-period (March and April, 2016). A healthy control group of thirty euthyroid was included. Blood samples were collected by vein puncture and serum was separated and stored at -20C. Adipokines: vaspin France), obestatin (Biomaghreb, (Biomerieux, Tunis), interleukin-6(Biolabo, France) & tumor necrosis factor- $\alpha$  (Biomerieux, France) were measured using ELISA method [5, 8, 9].

The results were analyzed statistically using analysis of variance test (ANOVA).Duncan test was used to find the significance between means in accordance to the program of SPSS version 19[12] at probability level p < 0.05.

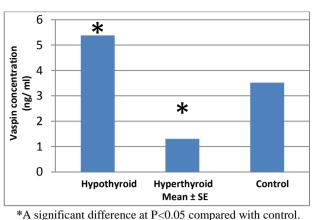
#### **Results and Discussion:**

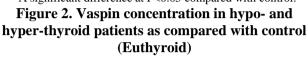
The findings show that a significant (p<0.05) increase in obestatin level in hypothyroid patients, while there is no significant difference in hyperthyroid patient compared with euthyroid people. The obestatin concentration means are  $30.84 \pm 3.17$ ,  $24.95 \pm 4.21$  and  $23.48 \pm 4.91$  pg/ ml in hypothyroid, hyperthyroid and euthyroid groups, respectively (Fig.1).



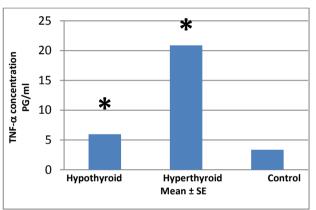


The results demonstrate a significant (p<0.05) increase in vaspin level concentration in hypothyroid patients compared with euthyroid group. The mean of vaspin concentration in hypothyroidism is  $5.38 \pm 2.13$  ng/ml while in euthyroid subjects is  $3.52 \pm 1.58$  ng/ml. In hyperthyroid patient, a significant (p<0.05) decrease is observed in vaspin level in comparison with the euthyroid group. In this group, the means of vaspin is  $1.30 \pm 0.18$  ng/ml (Fig. 2).



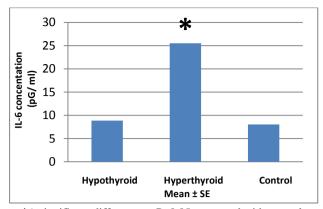


These results illustrated that there is a significant (p<0.05) increase in the TNF- $\alpha$ level in hypothyroid and hyperthyroid patients compared with the euthyroid subjects. The means of TNF- $\alpha$  levelwas 5.98 ± 1.57, 20.88 ± 2.92 and 3.37 ± 1.50 pg/ ml, respectively (Fig. 3).



\*A significant difference at P<0.05 compared with control. Figure 3. Tumor necrosis factor-αconcentration in hypo- and hyper-thyroid patients as compared with control (Euthyroid)

The results of this study explain a significant (p<0.05) increase interleukin-6 level in hyperthyroid patients, while there is no significant difference in hypothyroid patients compared with the euthyroid group. The IL-6 levels are 25.51  $\pm$  3.13, 8.85  $\pm$  1.54 and 8.01  $\pm$  2.28 pg/ ml in hyperthyroid, hypothyroid and euthyroid groups, respectively (Fig.4).



\*A significant difference at P<0.05 compared with control. Figure 4. Interleukin-6 concentration in hypoand hyper-thyroid patients as compared with control (Euthyroid)

It is thought that obestatin does not have any function by itself. However, its action on body composition is not still clear [11]. The association between thyroid disorders and obestatin levels was rarely investigated [13].

The possible state for obestatin findings in thyroid disease requires analytical study of these disorders in patients.Metabolic disorders could be responsible for serum obestatin alterations in hyperthyroid patients. Obestatin decrease may be associated with a transformation to high energy form[10]. Hypothyroidism is associated with high and hyperthyroidism is concerned with low levels of obestatin. It has been found a positive correlation between TSH levels and obestatin in hypothyroidism and suggested that obestatin may be a modulatory compound [11, 13].

The results of vaspin are in accordance with the results of [14] who found that vaspin concentrations are declined in hyperthyroid rats while they are elevated in hypothyroid rats compared with the normal control, suggesting that thyroid disease may influence vaspin expression.

It has been found that the lesion of thyroid gland may be related to these cytokines produced from immune system and lead to inflammatory responses. This reason might explain why interleukin- 6 is involved in hyperthyroid disorder [6].

An elevated prodution of adipose tissue to interleukin-6 has an effect on the level of other adipocytokines in hyperthyroid patients. Thus, IL-6 has an essential pathophysiological importance [14]. In hyperthyroid people, the increased level of IL-6 might be derived from intrathyroidal lymphocytes in those patients. Thus, in hypothyroidism, a decline in IL-6 level in intrathyroidal lymphocytes leads to a decrease in IL-6 concentration in the blood [5].

The chronic activation of the immune cells by releasing interleukins can cause constriction of the blood vessels directly or indirectly by producing C-

reactive protein which increases the chance of artherosclerosis in future [7].

The adverse effects of TNF in hyperthyroid patients suggested that TNF may mediate the alterations of hypothalamic-pituitary-thyroid (HPT) action. TSH activate iodide uptake by thyroid tissue and TNF inhibited action of TSH. In addition, TNF also inhibited iodide uptake in the absence of TSH [15].Therefore, thyroid gland has an effect on the regulation of tumor necrosis factor secretion [14].

In conclusion, interleukin-6 and tumor necrosis factor-  $\alpha$  increased in hyperthyroidism and decreased in hypothyroidism, while, obestatin and vaspin increased significantly in hypothyroid patients. Therefore, additional studies on other adipocytokines are required to determine the level of these cytokines in hypo- and hyperthyroid patients.

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# تعيين مستوى بعض السايتوكينات الدهنية في مرضى قلة وفرط افراز الدرقية في مدينة بغداد

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#### الخلاصة:

تم تعيين مستوى بعض السايتوكينات الدهنية (الاوبيستاتين و الفاسبين و عامل نخر الورم والانترلوكين-6)في مرضى قلة وفرط افراز الدرقية في مستشفى بغداد التعليمي في مدينة بغداد. اختير خمسون مريضا مصابين بقلة افراز الدرقية وخمسون مريضا مصابين بزيادة افراز الدرقية، اما مجموعة السيطرة فانها تضمنت ثلاثون شخص طبيعيين غير مصابين مصابين باختلال الدرقية، جمعت عينات الدم من الوريد وفصل وخزن مصل الدم بدرجة حرارة -20 درجة مئوية، وتم تقدير السايتوكينات الدهنية باختبار تحليل الامتصاص المناعي المرتبط انزيميا (الالبزا). اظهرت النتائج بان هناك ارتفاعا معنويا في معدلات الاوبيستاتين لمرضى قلة افراز الدرقية ولم يظهر أي فرق معنوي في مرضى فرط افراز الدرقية مقارنة مع مجموعة السيطرة. فضلا عن ذلك فان هذه الدراسة اوضحت بان هناك ارتفاعا معنويا في معدلات الفاسبين لمرضى قلة افراز الدرقية موانة مع مجموعة السيطرة. فضلا عن ذلك فان هذه الدراسة اوضحت بان هناك ارتفاعا معنويا في معدلات الفاسبين لمرضى قلة افراز الدرقية موانة مع مجموعة السيطرة. فضلا عن ذلك فان هذه الدراسة اوضحت بان هناك ارتفاعا معنويا في معدلات المناين لمرضى قلة افراز الدرقية موانة مع مادويا في مرضى فرط افراز الدرقية مقارنة مع مجموعة الاصحاء. علاوة على ذلك، فاك هن الفاسبين لمرضى قلة افراز الدرقية موانة مع مجموعة السيطرة فضلا عن ذلك فان مرضى فرط افراز الدرقية موانة مع مجموعة السيطرة فضلا عن ذلك فان هذه الدراسة اوضحت بان هناك ارتفاعا معنويا في معدلات الفاسبين لمرضى قلة افراز الدرقية وانخفاضا معنويا في مرضى قلة وفراز الدرقية مقارنة مع مجموعة السيطرة. كما ظهر أي نورة ارتفاعا معنويا في معدلات عامل نخر الورم لمرضى قلة وفرط افراز الدرقية مقارنة مع مجموعة السيطرة. كما ظهرت نتائج هذا البحث بان ومعاديات معنويا في معدلات عامل نخر الورم لمرضى قلة وفرط افراز الدرقية موانية مع مجموع السيطرة. فمار هو المرضي العام معنويا في مرضى في ارتفاع معنويا في معدلات علم معنويا في معدلات علم معنويا في معدلات عامل نخر الورم لمرضى قلة وفرط افراز الدرقية معارمة معنويا في مرضى قلة افراز الدرقية معارمة معنويا في معدلات عامل نخر الورم أمرضى قلة وفر افراز الدرقية ولم يظهر أي فرق معنوي في مرضى قلة افراز الدرقية معارم م معموعة السيطرة.

يستنتج من هذه الدراسة بان مستويات الانترلوكين-6 وعامل نخر الورم تعتبر مرتفعة في مرضى فرط افراز الدرقية ومنخفضة في مرضى قلة افراز الدرقية، بينما ترتفع مستويات الاوبيستاتين والفاسبين في مرضى قلة افراز الدرقية. لذا لابد من اجراء دراسات اضافية داخل جسم الكائن الحي ومختبريا لتأكيد هذه النتائج.

الكلمات المفتاحية: الأوبيستاتين، الفاسبين، عامل نخر الورم، الانترلوكين-6، فرط افراز الدرقية.