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Study the Effect of Some Adipokines and Interleukins in Hypo and Hyperthyroidism Patients

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Abstract

Introduction: Thyroid diseases have effects on metabolism and inflammation. Adipocytokines have autocrine, paracrine, and endocrine functions on several organs which have a central role in subclinical inflammation of adipose tissue, and obese adipose tissue secretes proinflammatory adipokines such as visfatin, and resistin. Cytokines play a role in the pathogenesis of several autoimmune thyroid diseases. **Methods:** All samples were conducted at Salah Aldeen General Hospital and the specific private clinic in Tikrit which started from November 2022 to February 2023, the study samples included (30) individuals with hyperthyroidism, (30) individuals with hypothyroidism, and (30) healthy individuals with age (18-76) years. **Results:** Adipokines (resistin and visfatin) and interleukins (IL10 and IL32) were increased in hypo and hyperthyroidism rather than control. **Conclusion:** The effect of inflammatory and anti-inflammatory response of some adipokines and interleukins affect the pathogenesis role in thyroid diseases.

Keywords: Thyroid diseases, Resistin, Visfatin, IL10, IL32.

INTRODUCTION

The thyroid gland is the largest organ that produces endocrine hormones. The activity of the thyroid gland is controlled by the hypothalamus-pituitary-thyroid axis. Thyrotropin-releasing hormone (TRH) secreted from the hypothalamus stimulates the synthesis and release of thyroid stimulating hormone/thyrotropin (TSH) from the pituitary gland¹⁻³.

Thyroid hormones regulate a wide array of metabolic parameters^{4,5}. Thyroid hormones regulate the body's energy balance and have effects on adipokine level. TSH receptors have been found in the adipose tissues, indicating that they play a role in the regulation of the adipocytokines which are involved in the regulation of energy balance⁶.

Resistin is a 12.5-kDa, cysteine-rich protein with 94-amino-acid polypeptide for 11 cysteine residues. It is a relatively new and poorly studied adipokine. It is secreted primarily by preadipocytes and less by mature preadipocytes of abdominal localization, but mainly produced by monocytes and macrophages. The relevance and physiological role of resistin in humans remain unclear. The studies reported different results of resistin concentration in patients with hyperthyroidism and hypothyroidism. Some studies have shown that resistin levels are increased in patients with hyperthyroidism and thyrotoxicosis, its concentration decreased with normalizing thyroid hormone status following treatment^{7,8}.

In other study, serum resistin levels in patients with Graves' disease decreased and on the other hand it in-

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creased in Hashimoto's and simple goiter patients. In recent years the role of resistin in thyroid function has been noticed and considered by researchers^{9,10}.

Visfatin is a 52 kDa adipocytokine with 491 amino acids, defined as the "pre-B cell enhancing factor (PBEF)" protein that stimulates B-lymphocyte formation in the bone marrow. Apart from adipose tissue, it is effective in various biological activities in a paracrine or endocrine manner expressed in hepatocytes, myeloblasts, immune cells, heart and pancreas. Accordingly, studies have focused on the potential role of visfatin in the pathogenesis of metabolic diseases and related complications¹¹. It has been reported that increased serum visfatin levels are associated with diseases such as obesity, diabetes and insulin resistance. Despite the contradictory results of recent studies showing that our understanding of Visfatin is still speculative, its secretion mechanism and physiological functions are not fully understood. Visfatin has been correlated with various inflammatory conditions, beta-cell functions, and cardiovascular diseases¹².

Interleukin-10 is a pleiotropic cytokine with both anti-inflammatory and anti-angiogenic properties that may be involved in the pathogenesis of autoimmune thyroid diseases. It is normally produced by activated T cells, monocytes, B cells, and thymocytes, contributing to antigenor mitogen-driven B cell differentiation, acting as a growth factor, and stimulating the humoral immune response¹³. It is an anti-inflammatory cytokine that maintains the balance of the immune response, allowing the clearance of infection while minimizing damage to the host. IL-10 can also dampen the harmful immune responses elicited in autoimmunity and allergy. The consequence of this activity, however, is that IL-10 can contribute to chronic infection. The importance of IL-10 in this balance is supported by a wealth of evidence gathered from studies in both the human and mouse systems^{14,15}.

Interleukin 32 (IL-32) is proinflammatory cytokine that in humans is encoded by the IL32 gene originally identified in human natural killer (NK) cells and T cells stimulated with IL-2 or mitogens, was initially called NK cell transcript 4 (NK4). It is expressed in endothelial cells, epithelial cells, and immune cells (NK cells, T cells, and dendritic cells). Recently, abnormal expression of IL-32 has been linked to various inflammatory or autoimmune diseases, including rheumatoid arthritis (RA)¹⁶, inflammatory bowel disease (IBD), systemic lupus erythematosus (SLE), allergic rhinitis, Behcet's disease, psoriasis and psoriatic arthritis¹⁷⁻²².

MATERIALS AND METHODS

The current study was conducted at Salah Aldeen General Hospital and the specific private clinic in Tikrit which started from November 2022 to February 2023, the study samples included (30) individuals with hyperthyroidism, (30) individuals with hypothyroidism, and (30) healthy individuals who do not suffer from thyroid diseases or any other diseases, and the ages of the study samples ranged between (18-76) years.

This study was approved by the Medical Ethics Committee of Tikrit University College of Medicine (*Code IQ.TUCOM.REC.2020.270710*). Ethical approval statements were acquired for all participated individuals, depending upon Helsinki Declaration of World Medical Association; with its last revision at Edinburgh in 2008.

Five ml of each blood sample was collected in plastic test tubes (plain tube) and then left for (20-30) minutes to clot the blood and separated by a centrifuge (5-15) minutes at a speed of 4000 rpm to obtain serum. The samples were stored in a deep freeze (-20 °C) for later hormonal tests: T3, T4, TSH, Resistin, Visfatin, IL10 and IL32 by Eliza method (sunlong company)²³.

The statistical analysis was carried out by using statistical program (SPSS 21) and comparison between groups which were made by using one-way analysis of variance (ANOVA), and tried out the arithmetic means for parameters by using test of Duncan multiple ranges. The level of statistical significance was taken at ($P < 0.05$).

RESULTS

The mean±SD of thyroid hormones levels (T3, T4 and TSH) were (3.49±0.86 ng/ml, 18.26±4.56 ug/dl and 0.31±0.25 IU/ml) respectively in patients with hyperthyroidism, but for hypothyroidism patients were (0.32±0.23 ng/ml, 2.05±1.37 ug/dl and 24.65±10.71 IU/ml) respectively when compared with control (1.16±0.33 ng/ml, 8.43±1.98 ug/dl and 2.56±1.68 IU/ml) respectively with a highly significant difference $P \leq 0.01$ as in table (1).

The mean±SD of serum Resistin levels was increased in hyper and hypothyroidism patients (4.36±2.11 and 5.02±2.28) ng/ml respectively when compared with control (2.96±0.62) ng/ml with a highly significant difference $P \leq 0.01$ but it increased in hypo rather than hyperthyroidism as in table (1).

The mean±SD of serum Visfatin levels was increased in hyper and hypothyroidism patients (5.84±2.86 and 7.57±3.09) ng/ml respectively when compared with control (1.53±0.58) ng/ml with a highly significant difference $P \leq 0.01$ but it increased in hypo rather than hyperthyroidism as in table (1).

The mean±SD of serum IL10 levels was increased in hyper and hypothyroidism patients (295.28±82.06 and 142.55±53.81) ng/ml respectively when compared

with control (110.5±40.5) ng/ml with a highly significant difference $P \leq 0.01$ but it increased in hyper rather than hypothyroidism as in table (1).

The mean±SD of serum IL32 levels was increased in hyper and hypothyroidism patients (341.26±124.8 and 433.98±180.6) ng/ml respectively when compared with control (36.46±10.2) ng/ml with a highly significant difference $P \leq 0.01$ but it increased in hypo rather than hyperthyroidism as in Table 1.

Table 1. Mean±SD for all parameter in hyper and hypothyroidism compared with Control.

Test	Hyperthyroidism	P value	Hypothyroidism	P value	Control
T3	3.49±0.86	$P \leq 0.01$	0.32±0.23	$P \leq 0.01$	1.16±0.33
T4	18.26±4.56	$P \leq 0.01$	2.05±1.37	$P \leq 0.01$	8.43±1.98
TSH	0.31±0.25	$P \leq 0.01$	24.65±10.71	$P \leq 0.01$	2.56±1.68
Resistin	4.36±2.11	$P \leq 0.01$	5.02±2.28	$P \leq 0.01$	2.96±0.62
Visfatin	5.84±2.86	$P \leq 0.01$	7.57±3.09	$P \leq 0.01$	1.53±0.58
IL10	295.28±82.06	$P \leq 0.01$	142.55±53.81	$P \leq 0.01$	110.5±40.5
IL32	341.26±124.8	$P \leq 0.01$	433.98±180.6	$P \leq 0.01$	36.46±10.2

$P \leq 0.01$ = highly significant

DISCUSSION

In this study, the results showed that some adipokines (Resistin and Visfatin) and interleukins (IL10 and IL32) increased in hypo and hyperthyroidism rather than control. Adipokines in our study increased in hypothyroidism rather than hyperthyroidism due to that they may play a role in insulin resistance, inflammation, and immunology in the pathogenesis of thyroid dysfunction and may be a potential marker of thyroid dysfunction and an effective therapeutic target²⁴.

Visfatin is supposed to have proinflammatory effects and a rise in serum levels was observed in autoimmune diseases²⁵, the changes of visfatin levels in thyroid disorders are also attributable to immunological mechanisms. It is suggested that visfatin can activate IL-6, and also IL-6 can stimulate visfatin gene expression²⁶.

Resistin is believed to have a role in insulin resistance and obesity. As a proinflammatory cytokine, it is

also believed to be related to inflammatory diseases independently from insulin resistance²⁷. The association between thyroid diseases and resistin levels is not well known.

IL10 was increased in hyperthyroidism rather than hypothyroidism while IL32 increased in hypothyroidism rather than hyperthyroidism due to small signaling proteins known as pro-inflammatory cytokines are up-regulated through inflammation because there is essential for starting and fostering inflammatory responses to illnesses²⁸.

IL-10 is an anti-inflammatory and immunosuppressive cytokine that influence the course of cancer by promoting immune escape through inhibition of the antitumor activity of immune cells²⁹. IL-10 is expressed in thyroid cancer and influence the aggressiveness of it. The immunosuppressive effect of IL-10 may be involved in the immune escape of thyroid cancer cells and promote the aggressiveness of thyroid cancer.

A large number of studies have shown that IL10 gene polymorphisms are associated with various diseases and play important roles in the pathophysiology and clinical courses of these diseases. However, studies are needed to explain the mechanisms of this process³⁰.

IL-32 has been found to be associated with various autoimmune diseases. IL-32 is a central mediator of both inflammatory and oncogenic pathways as reflected by its role in autoimmune, infectious and malignant diseases^{31,32}.

CONCLUSION

Adipokines and Interleukins were changed by thyroid diseases may be due to the effect of inflammatory and anti-inflammatory response of them.

References

- Hussein SZ. Evaluation of thyroid hormones and ferritin level in patients with β -thalassemia. *Med Pharm Rep.* 2022;95(2):152-157. doi: 10.15386/mpr-2053
- Rija FF, Hussein SZ, Abdalla MA. Osteoprotegerin, sclerostin, and osteocalcin serum levels in thyroid disorder patients. *Ukr Biochem J.* 2021;93(5):117-121. doi: 10.15407/ubj93.05.117
- Hussein SZ, Ali SJ. Evaluation of Serum thyroid hormones and cortisol in patients with chronic renal failure. *Tikrit Med J.* 2019;25(1):1-6.
- Hussein SZ, Farhan AS. Ferritin Level in Thyroid Diseases. 1st scientific conference of medical group colleges 26-27 March 2013: 21-25.
- Ali SJ, Hussein SZ. Evaluation of Serum Thyroid Hormones and Cortisol Level in Patients with Chronic Renal Failure. 1st scientific conference of medical group colleges 26-27 March 2013: 32-37.
- Cinar N and Alper G. Association between novel adipocytokines adiponectin, vaspin, visfatin, and thyroid: An experimental and clinical update. *Endocrine Connections.* 2013;2(4):30-38.
- Tripathi D, Kant S, Pandey S, Ehtesham NZ. Resistin in metabolism, inflammation, and disease. *FEBS J* 2020;287(15):3141-3149. doi: 10.1111/febs.15322
- Hammad MJ, Hassan ZL, Hussein SZ. Evaluation of some adipokines levels in pre and postmenopausal osteoporosis women. *HIV Nursing.* 2022;22(2):2345-2348.
- Yaturu S, Prado S, Grimes SR. Changes in adipocyte hormones leptin, resistin, and adiponectin in thyroid dysfunction. *J Cell Biochem* 2004;93(3):491-496. doi: 10.1002/jcb.20188
- Hammad MJ, Hassan ZL, Hussein SZ. The relation between some vitamins and homocysteine levels with pre and postmenopausal osteoporosis women. *HIV Nursing.* 2022; 22(2):2439-2442.
- Saboori S, Hosseinzadeh-Attar MJ, Hosseini M, Mirzaei K, Ahmadvand Z. The comparison of serum vaspin and visfatin concentrations in obese and normal weight women. *Diabetes & Metabolic Syndrome.* Clin Res Rev. 2015; 9(4):320-323.
- Farshchian F, Tehrani FR, Amirrasouli H, Pour HR, Hedayati M, Kazerouni F et al. Visfatin and resistin serum levels in normal-weight and obese women with polycystic ovary syndrome. *Inter J Endocrino Metabol.* 2014;12(3).
- Li MO, Flavell RA. Contextual regulation of inflammation: a duet by transforming growth factor-beta and interleukin-10. *Immunity.* 2008; 28: 468-476. doi: 10.1016/j.immuni.2008.03.003.
- Hussein SZ. The Relationship of Some Biochemical Markers with Inflammatory Prognosis in COVID-19 Patients. *Medicina Moderna.* 2022; 29(3):241-246. doi: 10.31689/rmm.2022.29.3.241
- Hussein SZ, Abdalla MA. Levels of Leptin, Adiponectin, and Insulin in COVID-19 Patients. *Medicina Moderna.* 2022; 29(1):89-92. doi:10.31689/rmm.2021.29.1.89
- Alsaleh G, Sparsa L, Chatelus E, Ehlinger M, Gottenberg JE, Wachsmann D, et al. Innate immunity triggers IL-32 expression by fibroblast-like synoviocytes in rheumatoid arthritis. *Arthritis Res Ther.* 2010 12:R135. doi: 10.1186/ar3073
- Shihan JT, Al-Janabi MSA, Abdalla MA. Impact of Aqueous Extract of Ginger and Chamomile Plant and Some Antihistamines in the Treatment of Drug-Allergy Induced in White Rats, a Physiological and Immunological Study. *HIV Nursing.* 2022;22(2):3449-3454.
- Rija FF, Hussein SZ, Abdalla MA. Physiological and immunological disturbance in rheumatoid arthritis patients. *Baghdad Sci J.* 2021;18(2):247-252. doi: 10.21123/bsj.2021.18.2.0247
- Nayaf MS, Ahmed AA, Abdalla MA. Alopecia areata and serum vitamin D in Iraqi patients: A case-control study. *Prensa Med Argent.* 2020;106(3):287. doi: 10.47275/0032-745X-287
- Shihan JT, Al-Janabi MSA, Abdalla MA. Drug allergy treatment induced in white rats mediated by the aqueous extract of chamomile plant, ginger and histidine drug: Immunological and physiological study. *Academia.* 2022;3(9):1-1. DOI: <https://doi.org/10.47134/academia.v3i9.552>
- Wang Y, Zhou B, Zhao Y, Yu X, Liu Y, Zhang L. Association of Plasma IL-32 Levels and Gene Polymorphisms with Systemic Lupus

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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- Erythematosus in Chinese Han Population. *Dis Markers*. 2016; 2016:2460206. doi: 10.1155/2016/2460206
22. Hussein SZ, Abdalla MA. Serum levels of alpha-melanocyte stimulating hormone, vitamin D, calcium, phosphorus and magnesium in COVID-19 patients. *Ukr Biochem J*. 2021;93(6):64-69. doi: 10.15407/ubj93.06.064
23. Sunlong Biotech Co. Human Elisa kit. Available from: <https://www.sunlongbiotech.com/gory.php?id=66>. [Accessed 2 December 2020]
24. Iglesias, Pedro, et al. Serum concentrations of adipocytokines in patients with hyperthyroidism and hypothyroidism before and after control of thyroid function. *Clin Endocrin*. 2003; 59(5):621-629.
25. Moschen AR, Kaser A, Enrich B and et al. Visfatin, an adipocytokine with proinflammatory and immunomodulating properties. *J Immuno*. 2007;178(3):1748-1758.
26. Yaturu S, Susan P and Sidney RG. Changes in adipocyte hormones leptin, resistin, and adiponectin in thyroid dysfunction. *J Cell Biochem*. 2004;93(3):491-496.
27. Abdalla MA, Nayaf MS, Hussein SZ. Evaluation of vitamin D in melasma patients. *Rev Romana Med Lab*. 2019;27(2):219-221. doi:10.2478/rrlm-2019-0023
28. Zádor F, Joca S, Nagy-Grócz G, Dvorácskó S, Szűcs E, Tömböly C, et al. Pro-Inflammatory Cytokines: Potential Links between the Endocannabinoid System and the Kynurenine Pathway in Depression. *Int J Mol Sci*. 2021 May 31; 22(11):5903. doi: 10.3390/ijms22115903.
29. Moore KW, de Waal Malefyt R, Coffman RL, O'Garra A. Interleukin-10 and the interleukin-10 receptor. *Annu Rev Immunol*. 2001; 19:683-765. doi:10.1146/annurev.immunol.19.1.683
30. Cunha LL, Morari EC, Nonogaki S, Marcello MA, Soares FA, Vassallo J, et al. Interleukin 10 expression is related to aggressiveness and poor prognosis of patients with thyroid cancer. *Cancer Immunol Immunother*. 2017; 66:141-148. doi:10.1007/s00262-016-1924-4
31. Abdalla MA, Nayaf MS, Hussein SZ. Correlation between serum α -MSH and vitamin D levels in vitiligo patients. *Iran J Dermatolgy*. 2020;23(4):163-167. doi: 10.22034/ijd.2020.120836
32. Kobayashi H, Lin PC. Molecular characterization of IL-32 in human endothelial cells. *Cytokine*. 2009;46:351-358. doi: 10.1016/j.cyto.2009.03.007