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. Thyrotropinreleasing 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 parameters4,5. 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 treatment7,8.

In other study, serum resistin levels in patients with Graves’ disease decreased and on the other hand it in-
Increased in Hashimoto’s and simple goiter patients. In recent years the role of resistin in thyroid function has been noticed and considered by researchers. 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 complications. 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 diseases.

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 response. 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 autoimmune 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. 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), inflammatory bowel disease (IBD), systemic lupus erythematosus (SLE), allergic rhinitis, Behcet’s disease, psoriasis and psoriatic arthritis.

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 it last revision at Edinburgh in 2008.

Five ml of each blood sample was collected in plastic test tubes (plan 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). 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 ≤ 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 ≤ 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 ≤ 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 ≤ 0.01 but it increased in hypothyroidism rather than hyperthyroidism.

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Hyperthyroidism</th>
<th>P value</th>
<th>Hypothyroidism</th>
<th>P value</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3</td>
<td>3.49±0.86</td>
<td>P ≤ 0.01</td>
<td>0.32±0.23</td>
<td>P ≤ 0.01</td>
<td>1.16±0.33</td>
</tr>
<tr>
<td>T4</td>
<td>18.26±4.56</td>
<td>P ≤ 0.01</td>
<td>2.05±1.37</td>
<td>P ≤ 0.01</td>
<td>24.65±10.71</td>
</tr>
<tr>
<td>TSH</td>
<td>0.31±0.25</td>
<td>P ≤ 0.01</td>
<td>24.65±10.71</td>
<td>P ≤ 0.01</td>
<td>2.56±1.68</td>
</tr>
<tr>
<td>Resistin</td>
<td>4.36±2.11</td>
<td>P ≤ 0.01</td>
<td>5.02±2.28</td>
<td>P ≤ 0.01</td>
<td>2.96±0.62</td>
</tr>
<tr>
<td>Visfatin</td>
<td>5.84±2.86</td>
<td>P ≤ 0.01</td>
<td>7.57±3.09</td>
<td>P ≤ 0.01</td>
<td>1.53±0.58</td>
</tr>
<tr>
<td>IL10</td>
<td>295.28±82.06</td>
<td>P ≤ 0.01</td>
<td>142.55±53.81</td>
<td>P ≤ 0.01</td>
<td>110.5±40.5</td>
</tr>
<tr>
<td>IL32</td>
<td>341.26±124.8</td>
<td>P ≤ 0.01</td>
<td>433.98±180.6</td>
<td>P ≤ 0.01</td>
<td>36.46±10.2</td>
</tr>
</tbody>
</table>

P ≤ 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 hyperthyroidism rather than hypothyroidism 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.

IL-10 was increased in hyperthyroidism rather than hypothyroidism while IL32 increased in hyperthyroidism 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 process\textsuperscript{30}. 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\textsuperscript{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**

2. 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/ubbj93.05.117

**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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