Evaluation Of Visfatin And Chemerin Levels In Patients With Hyperthyroidism

Malak Fadel Mahdi [1], Abbas Aboud Farhan[2], Roua Jamal Abdulkhaliq [3]

[1]Department of Biology, Collage of Education for Pure Science, University of Diyala, malakfadel@uomustansiriyah.edu.iq
[2]Department of Biology, Collage of Education for Pure Science, University of Diyala
[3]Department of Pathological Analysis, Collage of Applied Science, University of Falluiah, roua.jamal@uofallujah.edu.iq

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Abstract
Hyperthyroidism is a disease condition characterized by excessive production and secretion of thyroid hormones by the thyroid gland. The study aimed to evaluate levels of visfatin and chemerin in Iraqi individuals diagnosed with hyperthyroidism. A total of 60 patients diagnosed with hyperthyroidism were included in this study, consisting of 21 males and 39 females. The age of the patients ranged from 17 to 45 years and 30 healthy controls, consisting of 8 males and 22 females. Blood samples were obtained to measure the concentrations of visfatin and chemerin. The present results showed a significant increase ($P \leq 0.01$) in the concentration of visfatin (12.162± 7.171) compared with the control groups (1.584± 0.843ng/L). The present results also showed a significant increase ($P \leq 0.01$) in the concentration of chemerin which were (324.227± 297.055 ng/L) compared with the control groups (34.329± 23.917 ng/L and).

1- Introduction

Hyperthyroidism is characterized by the overproduction of thyroid hormones by the thyroid gland. Thyroid disorders such as hyperthyroidism have an incidence rate that varies from 0. 4 to 2. 5% in iodine-sufficient countries or regions of the world and an incidence of 40 per 100 000 in iodine-deficient areas (Censi et al., 2023).

The laboratory diagnosis of hyperthyroidism involves TSH measurement with serum T4 and T3 of thyroid hormones. T4 and T3 are elevated and TSH is decreased due to the supplementation (Wiersinga, Poppe & Effraimidis . ,2023).

The most common form of hyperthyroidism is Graves' disease (GD), which has a complex pathological progression. Graves' disease is primarily caused by (TSH) receptor antibodies. These antibodies attach to the TSH receptor on the follicular cells of the thyroid gland, leading to excessive secretion of thyroid hormone (TH) and increased excitability of multiple systems along with hypermetabolism. Typical symptoms of hyperthyroidism include palpitations, hand tremors, fatigue, and increased appetite along with weight loss, among others (Lee et al., 2024).

Chemerin, a newly identified adipokine, is secreted by adipose tissue and has received increasing research attention. This protein acts as a ligand that binds to the receptor CMKLR1, known as Chem R23 or GPCR-DEZ, in conjunction with a G protein. Chemerin is produced in organs involved in metabolic processes, including fatty tissue, liver, kidney, pancreas, lung, ovaries, and master gland. Chemerin derived from fatty cells acts as both an endogenous also exogenous factor. The relationship between chemerin and processes such as lipolytic activity, glucose intake, and biochemical routes remains to be investigated, as its exogenous response is closely linked to exogenous activity, which is associated with the chronic low-grade inflammation typical of obesity. The receptor CMKLR1, located on neutrophils and activated macrophages, and immune dendritic cells, acts as a receptor for chemerin, which was originally classified as a chemokine. Chemerin factor has been associated with adipogenesis, osteoclastogenesis, angiogenesis, and several health conditions such as type 2 diabetes, metabolic disorder, arthritis, Crohn's disorder, and hyperthyroidism (Şerefli et al., 2024).

Visfatin is an adipocytokine which has a molecular mass of 52kDa and is composed of 491 amino acid residues. Before developing its functions in the lymphatic system, it was officially known as the pre-B cell enhancing factor (PBEF) protein on account of it boosting the formation of B-lymphocytes in the bone marrow. Besides adipocyte, it acts in many biological proceedings in paracrine or endocrine manners in hepatocyte, myeloblast, immune cells, heart, and pancreas tissue. Thus, the focus of investigation has laid on the significance of visfatin in the progression of metabolic disorders and its outcomes. High serum visfatin concentration has been associated with obesity, type II diabetes and insulin resistance. Several studies have linked Visfatin with inflammation diseases, Beta-cell and cardiovascular diseases (RIJA, HUSSEIN& ABDALLA, 2023). The aim of the study was to the evaluation levels of visfatin and chemerin in Iraqi individuals diagnosed with hyperthyroidism.

2-Material and Method

This study comprised a total of 60 patients who were diagnosed with hyperthyroidism, consisting of 21 men and 39 females. The medical care for these individuals was provided at Baquba Teaching Hospital in Diyala and Balad Hospital in Salah al-Din, Iraq.The execution of this assignment spanned from January 2023 to April 2023. The age of the patients varied between 17 and 45 years. The consultant physicians diagnosed the existence of hyperthyroidism.A questionnaire was utilized to gather data about the patient's name, age, gender, and smoking habits. The study did not include individuals with heart disease, kidney failure, or those who were taking drugs for reducing high levels of lipids in the blood or antioxidants that impact oxidative stress.The study featured a representative, healthy group of 30 individuals, comprising 8 males and 22 females.The study involved collecting blood samples from each participant and separating the serum to measure the levels of chemerin and visfatin using sandwich Enzyme-Linked Immunosorbent Assay (ELISA). The SAS (2012) program was utilized for statistical analysis to identify the impact of various factors on study parameters. A T-test was employed to assess the statistical significance of the difference between means at a significance level of 0.01. The results were reported as the mean ± the standard deviation.

3- Results and Discussion

3-1 Measurement visfatin in hyperthyroidism patient and control group

The results showed current visfatin levels in the patients with hyperthyroidism and the control group. Patients in the hyperthyroidism group showed a statistically significant ($P<0.01$) rise in visfatin levels (12.162± 7.171 ng/ml) compared to the control group (1.584± 0.843). Table (3-1) Measurement visfatin in hyperthyroidism patient and control group.

Table (3-1) Measurement visfatin in hyperthyroidism patient and control group.

Statistical analysis		study Group		p-value
		patient	control	
Visfatin ng/ml	mean	12.162	1.584	0.000
	Std	7.171	0.843	

The study results showed a significant elevation in visfatin levels among hyperthyroid patients in comparison to the healthy control group. The reason for this could be an increase in visfatin levels as a compensatory response to the elevated metabolic rate caused by hyperthyroidism, which leads to a

faster breakdown of fat. Visfatin has been shown to have pro-inflammatory properties and elevated levels of this substance have been detected in individuals with autoimmune disorders(Łukawska-Tatarczuk et al.,2022)
The results agree with the study conducted by RIJA et al., 2023, which showed elevated levels of visfatin in hyperthyroid patients compared to individuals without thyroid disorders.
Additionally, the study revealed that individuals diagnosed with hyperthyroidism revealed significantly lower amounts of visfatin compared to those diagnosed with hypothyroidism. Patients diagnosed with hypothyroidism exhibited a notable reduction in plasma visfatin levels after undergoing treatment, while individuals with hyperthyroidism demonstrated a substantial elevation. The study conducted by Sharma and Kakadiya (2023) revealed a strong negative relationship between visfatin levels and fT3 and fT4 values, as well as a significant positive correlation with TSH levels.
Sawicka-Gutaj et al. (2021) conducted a recent study which revealed that in patients with hyperthyroidism, the presence of visfatin is mostly linked to the consumption of dietary fat, with a secondary influence from thyroid autoimmunity.
Shafiq conducted a study to examine the impact of visfatin on hyperthyroid patients who have dyslipidemia. The study found that the hyperthyroid group had markedly elevated levels of visfatin compared to the control group. The recorded elevations were accompanied by rises in other lipid indicators, such as total cholesterol, triglycerides, and LDL cholesterol. This study offers more understanding of the possible relationship
between visfatin and lipid metabolism in the context of thyroid disease (Shafiq, 2019).
Sheikh et al., 2019 discovered that hyperthyroid individuals exhibited reduced levels of visfatin compared to the control group. The study discovered that hyperthyroidism influences the concentrations of these adipokines. The adipokines have also demonstrated correlations with different thyroid hormones (Alshaikh et al., 2019). Increased concentrations of visfatin have been detected in various chronic inflammatory disorders, such as rheumatoid arthritis and chronic intestinal mucosal inflammation, including ulcerative colitis, Crohn's disease, and thyroid illness (Sotak et al., 2021).
Visfatin is an adipokine that was previously recognized as a growth factor for early B-lymphocytes and referred to as a pre-B cell colony-enhancing factor (Tabandeh et al.,2023).Clinical investigations have shown that the group with hyperthyroidism had noticeably elevated levels of plasma visfatin compared to the control group. Additionally, visfatin levels had a considerable drop following the study. Management of hyperthyroidismThe elevated levels of visfatin in hyperthyroidism may be associated with visfatin resistance (Mishra et al,.2018).
Visfatin interacts with the insulin receptor at a distinct location from insulin, leading to hypoglycemia by promoting the usage of glucose in fat cells and muscle cells, while also decreasing the release of glucose from the liver (Mostafa Ahmed, et al., 2019).
Visfatin is a cytokine that has a physiological impact on lowering plasma glucose levels (Dakroub et al., 2022).

3-2 Measurement chemerin in hyperthyroidism patient and control groups
Results of the present study demonstrated an increase in chemerin levels in both individuals with hyperthyroidism and the control group. The chemerin levels in hyperthyroid individuals (324.227± 297.055 ng/L) showed a highly significant increase ($P<0.01$) compared to the control group (34.329± 23.917). Table (3-2) the measurement of chemerin in both hyperthyroidism patients and the control group.

Table (3-2) The measurement of chemerin in hyperthyroidism patient and control group.

Statistical analysis	study Group		p-value
	patient	control	

Chemerin ng/I	**mean**	**324.227**	**34.329**	**0.000**
	std	**297.055**	**23.917**	

The results of the present study demonstrated that the levels of chemerin were higher in patients with hyperthyroidism in comparison to the control group. The heightened chemerin levels observed in individuals with hyperthyroidism may be associated with the amplified metabolic activity and inflammation caused by excessive thyroid hormone synthesis. These hormones impact adipose tissue and other tissues, resulting in an
elevation in chemerin production as part of the body's metabolic and inflammatory response (Tabandeh et al.,2023).

The results of this study agree with the research conducted by Tabandeh et al. in 2023, which reported increased levels of chemerin in people diagnosed with hyperthyroidism. Chemerin acts as a pro-inflammatory adipocytokine by stimulating the production of inflammatory cytokines like TNF-α and IL-6.

Alshaikh et al., (2019) found that patients with hyperthyroidism had significantly higher levels of chemerin compared to the control group.

Chemerin is involved in the early stage of acute inflammation and its suppression occurs through its interaction with the ChemR23 receptor. The main role of this adipokine is to activate macrophages and trigger chemotaxis in immature dendritic cells. The concentrations of chemokines in the blood serum exhibit a robust correlation with many indicators of inflammatory response, such as tumor necrosis factor-alpha (TNF-α), interleukin 6 (IL-6), and C-reactive protein (Su et al., 2021).

A further study was conducted to investigate the levels of chemerin in cases with Subhyper and Subhypo. Patients diagnosed with Sub Hypo exhibited significantly higher levels of chemerin in their bloodstream compared to patients diagnosed with SubHyper. Patients with Subhyper exhibited a significant decrease in serum chemerin levels compared to healthy persons. Although the chemerin levels in patients with SubHypo were higher than those in healthy controls, the study conducted by Tamer et al. (2021) did not observe a statistically significant difference.

In their 2019 study, Al Doghaither et al. The study found increased chemerin levels in people diagnosed with hyperthyroidism. Hyperthyroidism is believed to affect adipose tissue function due to the similar physiological effects of adipokines and thyroid hormones on energy expenditure, as well as their role in regulating glucose and lipid metabolism. This can potentially result in additional metabolic issues.

Amiri, Tabandeh, and Hosseini conducted a study in 2021. Chemerin, resistin, and visfatin were identified as adipocytokines produced by adipose tissue in this study. Previous research has recorded changes in the levels of these adipocytokines in persons who have diabetes or thyroid disease.

Chemerin is a chemical compound that plays a crucial function in the interference of metabolic processes and is mostly secreted by adipose tissue. Studies have demonstrated a favorable correlation between chemerin and inflammatory markers in overweight persons diagnosed with type 2 diabetes (T2D). The Chemerin level is considered a dependable marker of insulin resistance level (Ergün et al., 2023).

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