



The Influence of Thyroid Hormones on Levels of Lipid Profile and Adipokine in Iraqi Women with Thyroid Disorders

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Abstract

Hypothyroidism and hyperthyroidism are prevalent endocrine diseases. These have significant implications for lipid synthesis, mobilization, and metabolism. Retinol-binding protein 4 is a new adipokine implicated in some physiological and pathological processes, such as metabolic and endocrine disorders. Its elevation aids in the diagnosis of thyroid problems. The present study includes 60 women with thyroid diseases; 30 of them have hypothyroidism and 30 have hyperthyroidism. This study includes 20 healthy women as a control group. For each participant anthropometric, biochemical Thyroid-stimulating hormone, triiodothyronine, Thyroxine, lipid profile, and retinol binding protein-4 are measured. The results show that hypothyroid women have significantly higher levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol as compared to the hyperthyroid or control group. The serum of total cholesterol, triglycerides, and low-density lipoprotein cholesterol are significantly lower in hyperthyroid women compared to the hypothyroid or control group. In addition, there are no significant differences in blood high-density lipoprotein cholesterol concentrations among the three groups. Furthermore, serum retinol-binding protein-4 levels were higher in the hyperthyroid group compared to the hypothyroid or control groups. According to the findings of this study, hypothyroidism causes dyslipidemia, which raises the risk of cardiovascular disease while hyperthyroidism causes abnormalities in lipid profiles. Additionally, hyperthyroidism causes an increase in serum retinol-binding protein-4 levels in the blood.

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1. Introduction

In the human body, the most crucial endocrine organ is the thyroid gland [1]. It situates near the base of the neck, at the front of the trachea, and below the Adam's apple [2]. Both tri-iodothyronine (T3) and thyroxine (T4) are produced and stored by the thyroid gland [3]. These hormones are responsible for the regulation of carbohydrate, fat, and protein metabolism [4]. Hyperthyroidism is caused by an excess of thyroid hormone synthesis and release [5]. While hypothyroidism is caused by insufficient production of thyroid hormones generated by the thyroid gland [6]. Thyroid hormones have an impact on lipid synthesis,

mobilization, and breakdown; however, synthesis is more stimulated than degradation. The main and best-known impacts on lipid metabolism are increase lipid substrate consumption, increase adipose tissue fat production, and mobilization, increase non-steroid fatty acid (NEFA), and enhance lipoprotein-lipase activity [7]. Adipose tissue releases several types of bioactive compounds known as adipokines, including peptides/proteins, immunological molecules, and inflammatory mediators [8]. Adipokines are biological mediators that perform crucial functions in maintaining energy homeostasis, regulating appetite, managing glucose and lipid metabolism,

enhancing insulin sensitivity, promoting angiogenesis, modulating immune function, and controlling inflammation. These functions are achieved via endocrine, paracrine, and autocrine mechanisms [9]. Retinol-binding protein-4, also known as RBP-4, is an adipokine that is mainly produced by adipose tissue, liver and, to varying degrees, in other organs like the kidneys, lungs, brain, retina, and testes [10]. One of RBP-4's primary functions is to transport retinol to tissues for biological action [11]. RBP-4 has been identified as a factor involved in a range of human diseases, such as impaired vision and ocular diseases, disorders related to glucose and lipid homeostasis, as well as cardiovascular diseases [12]. In addition to serving as an indicator of obesity and insulin resistance, RBP-4 is also recognized as a marker of inflammation [13]. The primary objective of this study is to examine the impact of thyroid disorders on levels of retinol-binding protein-4, as well as to investigate the relationship between lipid profiles and thyroid hormones in Iraqi women diagnosed with thyroid disorders.

2. Materials and Methods

2.1. Study subjects

The present work involved 60 women with thyroid disorders who were split into two groups: 30 with hypothyroidism and 30 with hyperthyroidism. The age of women in both groups is 20-40 years old. Twenty healthy females in the same age range were involved as the control group. Participants were recruited from the National Diabetes Centre at Al-Mustansiriyah University in Baghdad City.

2.2. Exclusion criteria

The current study excluded women who had the following conditions: smoking, diabetes mellitus, heart failure, hypertension, neoplasms, pregnancy, renal or hepatic disease, and patients who are taking medication other than carbimazole or levothyroxine, which may affect adipokine concentrations.

2.3. Sample collection

Specimens of 5 millilitres of blood were collected from patients and healthy women who had fasted for 8–12 hours overnight. The blood samples were collected in gel tubes and allowed to coagulate for fifteen minutes. Blood samples were centrifuged at 3000 rpm for 15 minutes at room temperature to separate the serum. Aliquots of the extracted serum were frozen at -60 °C until analysis.

2.4. Calculating Body Mass Index (BMI)

BMI was calculated for each participant by dividing their weight (in kilograms) to their squared height (in meters, m).

2.5. Biochemical analysis

Serum total thyroid function was measured using the electro-chemi-luminescence method on a hormonal analyzer (autoanalyzer Cobas E411, Roche, Germany). Serum lipid profile concentrations were also evaluated using a semi-automatic chemical analyzer (Humalyzer primus, Human, Germany). Serum adipokine concentrations were measured using an enzyme-linked immunosorbent assay (ELISA) kit.

2.6. Statistical Analysis

The demographic and biochemical data for the present investigation were analyzed by GraphPad Prism software, version 7.04 (San Diego, California, USA). One-way ANOVA was used to determine the means, standard deviations (STD), and significant differences (P-value) between the means of the three groups. ($P < 0.05$) was statistically significant, ($P < 0.0001$) was regarded as extremely statistically significant.

3. Results and Discussion

The results illustrate demographic data and biochemical markers in healthy (Group 1), hypothyroid (Group 2), and hyperthyroid (Group 3) Table 1. The demographic data revealed that there was a significant difference in BMI between hypothyroid, control, and hyperthyroid groups ($p < 0.0001$). There was a significant difference in T3, T4, and TSH among all groups ($p < 0.0001$). Regarding lipid profiles (total cholesterol TC, triglyceride TG, low-density lipoprotein cholesterol LDLC, and high-density lipoprotein cholesterol HDLC), there was also a significant difference between hyperthyroid hypothyroid and healthy groups ($P < 0.0001$). Although there were no significant differences in blood high-density lipoprotein cholesterol levels among the three groups ($p = 0.1203$). Of interest, the serum concentration of retinol-binding protein-4 was extremely significant in the hyperthyroid group compared with two other groups ($p < 0.0001$) Figure 1.

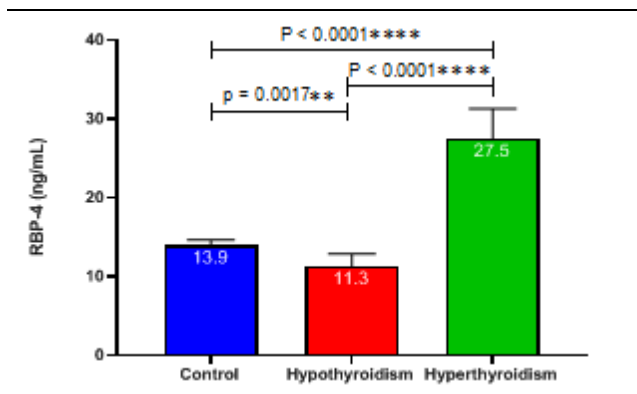


Figure 1. RBP-4 (ng/mL) comparison between the hypothyroidism, hyperthyroidism, and control groups.

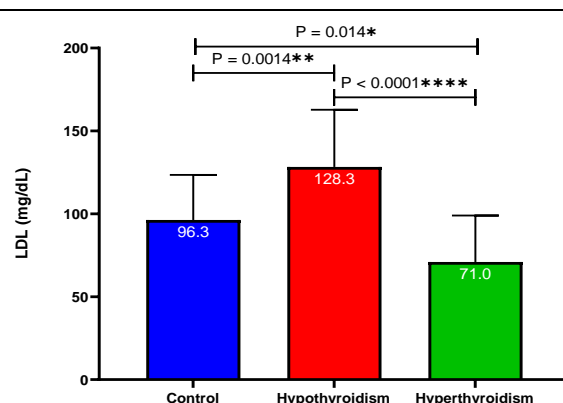


Figure 4: LDL (mg/dL) comparison between the hypothyroidism, hyperthyroidism, and control groups.

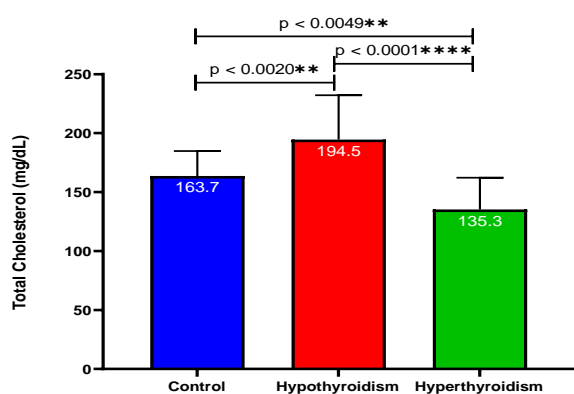


Figure 2: TC (mg/dL) comparison between the hypothyroidism, hyperthyroidism, and control groups.

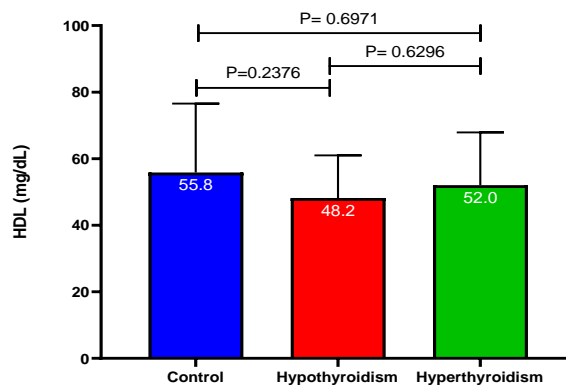


Figure 5: HDL (mg/dL) comparison between the hypothyroidism, hyperthyroidism, and control groups.

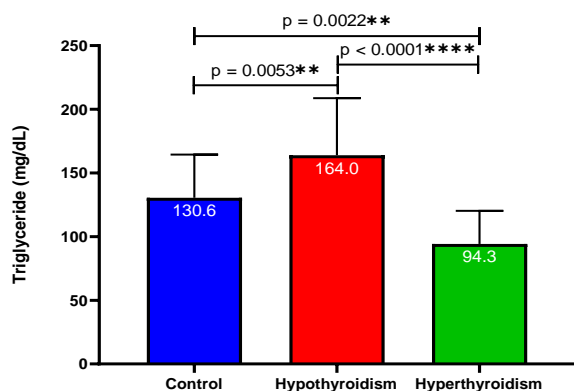


Figure 3: TG (mg/dL) comparison between the hypothyroidism, hyperthyroidism, and control groups.

Thyroid hormones regulate several body processes. They increase heat production and resting metabolic rate, influence cell division and development, regulate how other hormones are responded to, and modify lipid and glucose metabolism [14]. The outcomes of this study indicate that T3 and T4 levels significantly increased while TSH levels significantly reduced when hypothyroidism compare to the control group. On the other hand, T3 and T4 levels in hypothyroid women were significantly low, but TSH levels were higher than in the control group. The results of this research is closely resemble the findings of previous investigations [15]. The most frequent causes of hypothyroidism include Hashimoto's thyroiditis, medication side effects, irregular thyroid growth, pituitary abnormalities, and genetic defects. Usually, hyperthyroidism generates too much thyroid hormone. It can be caused by an autoimmune condition called Graves'

disease, an excess of iodine in the body, or an overdose of synthetic thyroid hormone [16]. The present investigation found that RBP4 levels were significantly lower in hypothyroid female patients than in healthy controls. The results obtained in this study are consistent with the findings of earlier research [17]. A possible explanation for this might be that medical treatments that enhance thyroid function may reduce RBP-4 levels in the blood. The concentration of RBP-4 in hyperthyroid female patients was significantly greater than in the control group. This outcome corresponds with an earlier study [18]. Serum

RBP-4 levels are raised in people with Graves disease and rise as the condition worsens. Additionally, inflammatory markers like CXCL-13 and interleukin-6 (IL-6) were found to have a positive correlation with RBP-4 levels. The subsequent investigation revealed the cause of the elevated RBP-4 levels in hyperthyroidism that could be linked to the control of inflammation. As a result, cytokines and other inflammatory mediators may increase the levels of RBP-4. This increase may be the result of inflammation which is brought on by hyperthyroidism [19].

Table 1. Demographic data and biochemical markers of the hypothyroidism, hyperthyroidism, and control groups.

Parameter	Control	Hypothyroidism	Hyperthyroidism	p-value	Sign
BMI (kg/m²)	24.39±3.40 ^a	28.23±4.63 ^b	21.38±2.26 ^c	<0.0001	HS
TSH (uIU/mL)	2.19±0.52 ^a	9.15±2.37 ^b	0.12±0.02 ^c	<0.0001	HS
T3 (nmol/mL)	2.10±0.41 ^a	1.52±0.35 ^b	2.72±0.39 ^c	<0.0001	HS
T4 (nmol/mL)	95.56±15.67 ^a	75.92±8.97 ^b	131.1±9.91 ^c	<0.0001	HS
TC (mg/dL)	163.7±21.16 ^a	194.5±37.60 ^b	135.3±26.88 ^c	<0.0001	HS
TG (mg/dL)	130.6±33.88 ^a	164.0±44.75 ^b	94.27±25.98 ^c	<0.0001	HS
HDL (mg/dL)	55.84±20.72 ^a	48.20±12.79 ^a	52.04±15.83 ^a	0.1203	NS
LDL (mg/dL)	96.29±27.16 ^a	128.28±34.48 ^b	70.98±28.01 ^c	<0.0001	HS
RBP-4 (ng/mL)	13.94±0.67 ^a	11.32±1.50 ^b	27.51±3.80 ^c	<0.0001	HS

Mean±SD, Standard Deviation. **S**: “significant”, p-value < 0.05; **NS**: “no significant”, P-value> 0.05; **HS**: “high significant”, p-value< 0.0001. The three letters (a, b, and c) in the same row in the tables indicate significant differences in a parameter between groups.

In our study, the prevalence of dyslipidemia was found in hypothyroidism. In contrast, hyperthyroidism showed a significant decrease in lipid profile. A hypermetabolic state, which are brought on by hyperthyroidism, is marked by elevated resting energy expenditure, decreased cholesterol levels, weight loss, increased gluconeogenesis and increased lipolysis. Contrarily, hypometabolism, which is represented by higher cholesterol levels, reduced lipolysis, decreased gluconeogenesis, and lower resting energy expenditure, is linked to hypothyroidism

[20]. The findings of the current study indicate that hypothyroidism group had elevated levels of cholesterol, triglycerides, and LDL but no significant increase in HDL. The outcomes in this study are in agreement with those reported in earlier investigations [21]. There are several possible explanations for this result. Thyroid hormones have a significant role in the metabolism of triglycerides and cholesterol. When thyroid hormone levels are low in hypothyroidism, lipoprotein lipase (LPL), an enzyme that clears TG-rich lipoproteins, is less active, which raises

TG levels in the blood [22]. Simultaneously, reduced thyroid hormones result in lower LDL receptor expression, which may restrict the absorption of LDLC from circulation and LDLC catabolism, ultimately leading to higher levels of circulating TC [7]. According to the findings of the present research, the hyperthyroidism group had a significant decrease in triglyceride, LDL, and total cholesterol compared to the healthy group. The results obtained in this investigation are in agreement with the findings of earlier research [23]. This result might be explained by the fact that when thyroid hormone levels are high, the body's metabolic rate increases, leading to increased activity of lipoprotein lipase. This can lead to a decrease in triglyceride levels [24]. Additionally, stimulation of the hepatic lipase could be another reason. Hepatic lipase is responsible for breaking down LDL cholesterol (the "bad" cholesterol) into smaller particles that can be removed from the bloodstream more easily. Furthermore, stimulation the production of more LDL receptors in the liver allows for more LDL cholesterol to be removed from the bloodstream. This further contributes to decrease in TC with increased thyroid hormone levels [25]. Thyroid dysfunction can lead to cardiovascular disorders by altering lipid profiles. Thus, screening for these factors can lower the risk of cardiovascular disease in people with low thyroid hormone levels [26].

4. Conclusions

The lipid profile is significantly impacted by thyroid disorders. We conclude that hypothyroidism induces dyslipidemia, which could be further increase the risk of cardiovascular disease. while hyperthyroidism causes abnormalities in lipid profiles. Additionally, hyperthyroidism causes an increase in serum retinol-binding protein-4 levels in the blood.

References

- [1] Prabal, P.; Alfredo, I.; Elmer, J. G. A.; Nazila, E.; Sathish, B.; Michael, F.; "Thyroid ultrasound texture classification using autoregressive features in conjunction with machine learning approaches". *IEEE Access*, 7: 79354–79365, 2019.
- [2] Rajani, S.; "Surgical Anatomy of Thyroid Gland A Comprehensive Review". *Basic Sci. Med.* 9 (1): 10–14, 2020.
- [3] Ceyhun, B.; Ajay, P.; "Plasticizers: negative impacts on the thyroid hormone system". *Environ. Sci. Pollut. Res.*, 29 (26): 38912–38927, 2022.
- [4] Santanu, M.; Debasish, M.; Karuppusamy, R.; Govindasamy, M.; "Halogen bonding in biomimetic deiodination of thyroid hormones and their metabolites and dehalogenation of halogenated nucleosides". *Chem. Bio. Chem.*, 21(7): 911–923, 2020.
- [5] Zainab, A.M.; Shaima, R.I.; Aida, H.I.; "A correlation study between hyperthyroidism and some apoptosis markers among Iraqi patients". *Iraqi . J. Sci.*, 62 (5): 1484–1493, 2021.
- [6] Abeer, C.Y.A.; "An evaluation of blood glucose and lipid profile in female hypothyroidism patients in Kerbala province, Iraq". *Biomed.*, 42 (3): 556–560, 2022.
- [7] Waled, A.H.; Azab, E.; Laila, H.F.S.; "Correlation between Hypothyroidism, Hyperthyroidism and Lipid Profile in Thyroid Dysfunction Patients". *Clin. Med. J.*, 4 (2): 6–14, 2018.
- [8] Daniel, A.; Gabriela, H.; Bárbara, R.; Janette, F.; "Adipokine contribution to the pathogenesis of osteoarthritis". *Mediators Inflamm.*, 2017, 2017.
- [9] Pierre, S.M.; Zeina, A.; Pousette, F.H.; Syeda, S.H.; Cesar, A.P.; "Adipocytokines: Are they the Theory of Everything?". *Cytokine*, 133, 2020.
- [10] Pamela, A.N.; Matthias, B.; "Retinol-binding protein 4 in obesity and metabolic dysfunctions". *Mol. Cell. Endocrinol.*, 531: 111312, 2021.
- [11] Thomas, O.; Rune, B.; "Retinol, Retinoic Acid, and Retinol-Binding Protein 4 are Differentially Associated with Cardiovascular Disease, Type 2 Diabetes, and Obesity: An Overview of Human Studies". *Adv. Nutr.*, 11(3): 644–666, 2020.
- [12] Julia, S.S.; Achim, L.; Michael, S.; "Biological functions of RBP4 and its relevance for human diseases". *Front. Physiol.*, 12, 659977, 2021.
- [13] Suman, T.; Nirupama, D.; Devi Prasad, P.; Rasmita, K.P.; Sucheta, P.; Sudipta, O.; "Role of Serum Retinol Binding Protein 4 (RBP4) Concentration in Patients with Primary Hypertension: A Case-control Study". *J. Clin. Diagnostic Res.*, 16(10): BC18-BC21, 2022.
- [14] Yanyan, C.; Xiafang, W.; Ruirui, W.; Xiance, S.; Boyi, Y.; Yi, W.; Yuanyuan, X.; "Changes in profile of lipids and adipokines in patients with newly diagnosed hypothyroidism and hyperthyroidism". *Nat. Publ. Gr.*, 6, 1–7,

- 2016.
- [15] Hussein, M.O.; Athmar, J.A.A.; Suhad, R.M.; "Comparing the Concentrations of Thyroid Stimulating Hormone and Thyroid Hormone in Females with Hypothyroidism and hyperthyroidism in Iraq". *J. Pharma. Negat. Result.*, 13(3): 878-880, 2022.
- [16] Payman, A.H.; Saeed, K.H.; Sana, M.A.; "Evaluation of Thyroid stimulating hormone and thyroid hormone concentrations in females with hypothyroidism and hyperthyroidism". *Rafidain J. Sci.*, 28(4): 1-7, 2019.
- [17] Eiman, A.A.A.; Warka'a, T.A.; Mezher, N.M.; "A comparative study of retinol-binding protein-4 and progranulin in iraqi women with thyroid disorder". *Int. J. Drug Deliv. Technol.*, 11(1): 36-41, 2021.
- [18] Yanqin, H.; Yue, S.; Yuxuan, H.; Qiuxia, L.; Fan, R.; "Serum Levels of CXCL-13, RBP-4, and IL-6, and Correlation Analysis of Patients with Graves' Disease". *Emerg. Med. Int.*, 2022, 2022.
- [19] Yaccil, A.F.; Martha, I.B.; Juan, M.M.; Cecilia, C.G.; Eugenia F.; and Mónica, E.; "Interplay of retinol binding protein 4 with obesity and associated chronic alterations". *Mol. Med. Rep.*, 26 (1): 1-12, 2022.
- [20] Rashmi, M.; Yan-Yun, L.; Gregory, A.; "Thyroid hormone regulation of metabolism". *Physiol. Rev.*, 94, 355-382, 2014.
- [21] Divya, U.; Jean, M.; Geetha, N.; "Association of insulin resistance and lipid profile with serum T3, T4, and TSH in patients with hypothyroidism". *Natl. J. Physiol. Pharm. Pharmacol.*, 13(3): 499-503, 2023.
- [22] Huixing, L.; Daoquan, P.; "Update on dyslipidemia in hypothyroidism: the mechanism of dyslipidemia in hypothyroidism". *Endocr. Connect.*, 11(2): e210002, 2022.
- [23] Azhar, Y.D.; Abeer, A.A.A.; "Estimation of Visfatin, Adiponectin Hormone and Lipid Profile in Hyperthyroidism Patients". *Ann. Rom. Soc. Cell Biol.*, 25 (4): 5617-5626, 2021.
- [24] Jeongmin, L.; Jeonghoon, H.; Kwanhoon, J.; Dong-Jun, L.; Jung-Min, L.; Sang-Ah, C.; Moo-Il, C.; Min-Hee, K.; "High normal range of free thyroxine is associated with decreased triglycerides and with increased high-density lipoprotein cholesterol based on population representative data". *J. Clin. Med.* 8 (6): 758, 2019.
- [25] Mahmood, S.M.; Measer, A.A.; "Effect of Hyperthyroidism on Lipid Metabolism and Evaluation of the Protective Role of Pomegranate Juice against the Risk of Oxidative Stress in Albino Rats". *Int. J. Drug Deliv. Technol.*, 12 (1): 373-378, 2022.
- [26] Gopalakrishnan, M.; Ramidha, P.; Vinitha, V.; "Comparative study of lipid profile anomalies in thyroid dysfunction". *Natl. J. Physiol. Pharm. Pharmacol.*, 12(9):1366-1370, 2022.