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Evaluation of some Biochemical Parameters in Iraqi Patients with Hyperthyroidism

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Abstract: Hyperthyroidism is autoimmune disease that is considered a thyroid gland problem. A clinical condition known as hyperthyroidism is defined by the thyroid gland producing and secreting an excessive amount of thyroid hormones. Lipid profile play an essential role in the progression and development of hyperthyroidism. The aim of this study is to evaluate the level of some biochemical parameters in Iraqi patients with hyperthyroidism. Sixty hyperthyroid patients and 30 healthy individuals with age range from (30-65) years were enrolled in this study during their attendance at the National Center for Diabetes Treatment and Research in Baghdad from the period between December 2021 to April 2022 .Blood samples were collected to evaluate the level of thyroid hormone like triiodothyronin (T3), thyroxin (T4) and thyroid stimulating hormone (TSH) using ELISA technique, and total cholesterol (TC), triglycerides (TG), high- density lipoprotein cholesterol (HDL-C) were measured spectrophotometrically by using different type of kits. The results showed highly significant ($p \leq 0.01$) increase in the level of T3, T4 in the patients with hyperthyroidism in comparison with the control group, While, TSH level showed highly significant ($p \leq 0.01$) decrease in the patients with hyperthyroidism as compared with control group. The level of TC, HDL-C and LDL-C showed a highly significant ($p \leq 0.01$) decrease in the patients with hyperthyroidism in comparison with the control group, While, the level of TG and VLDL-C showed a highly significant ($p \leq 0.01$) increase in the patients with hyperthyroidism in comparison with the control group. It can be concluded that the lipid profile play a major role in the pathogenicity of hyperthyroidism.

Keywords: Hyperthyroidism, T4, TSH, Lipid profile.

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Introduction

Hyperthyroidism defined as a condition characterized by increased thyroid hormones synthesis and secretion from the thyroid gland (1). The prevalence of hyperthyroidism is 0.8% in Europe (2). And 1.3% in the USA (3).The laboratory diagnosis for hyperthyroidism is based on serum thyroid-stimulating hormone (TSH) measurement along with serum hormones (T4) and (T3). The levels of T4 and T3 are high, while TSH levels are low (4).

The typical signs of hyperthyroidism are weight loss despite increased appetite, tachycardia, restlessness, tremor, weakness and heat intolerance (5). Other symptoms of hyperthyroidism were considered, including nervousness and irritability, sweating, insomnia and diarrhea (6).

Subclinical hyperthyroidism can be classified as endogenous and exogenous causes: The endogenous, the most common cause of endogenous subclinical hyperthyroidism is release of excess thyroid hormone by the thyroid gland, while the exogenous causes of it include treatment with levothyroxine, exogenous iodine exposure (7). The major cause for this acquired condition is due to chronic autoimmune thyroiditis (inflammation of the gland). Some other secondary

causes can be due to treatment for hyperthyroidism, removal of thyroid gland, and some radiation treatments for certain cancers (8, 9).

Thyroid hormones (THs) are iodinated peptides synthesized and stored by the thyroid gland. Their structure is identical in all vertebrates, and most of their functions have also been conserved throughout vertebrate evolution (10). The thyroid hormones are derived from the amino acid tyrosine and produced by the thyroid gland in response to stimulation by the thyroid-stimulating hormone (TSH) produced by the anterior pituitary (11).

Thyroid-stimulating hormone, also known as TSH, is a glycoprotein hormone produced by the anterior pituitary (12). When TSH binds to the receptor on the thyroid cells, this stimulates these cells to produce T4 and T3, and release them into the bloodstream, these hormones have a negative effect on the pituitary gland, and stop the production of TSH if the levels of T4 and T3 are too high. They also switch off production of a hormone called TRH. This hormone is produced by the hypothalamus and it also stimulates the pituitary gland to make TSH (13).

Hyperthyroidism may result from increased synthesis and secretion of T4 and T3 from the thyroid, caused by thyroid stimulators in the blood or by autonomous thyroid hyperfunction. It can also result from excessive release of thyroid hormone from the thyroid without increased synthesis. Such release is commonly caused by the destructive changes of various types of thyroiditis (14).

Hyperthyroidism can also be the underlying cause of unexpected improvement of lipid profile in hyperlipidemic patients (15). It leading cause of mortality worldwide is cardiovascular diseases, many of which are conditioned by persistent elevated lipid levels in the blood; the literature reports that more than 30% of the world's population suffers from dyslipidemia, and a very important cause of dyslipidemia is thyroid hormone dysfunction (16).

The purpose of the present study was to estimate of some biochemical parameters in Iraqi patients with hyperthyroidism.

Material and methods

Sixty patients (men and women) with hyperthyroidism after diagnosed by the physician and thirty apparently healthy subjects with the same age range (30 to 65) years old were included in the study through their attendance to National Center for Diabetes Treatment and Research in Baghdad during the period between December 2021 to April 2022. The necessary information were taken from all subjects after taking their permission depending on the letter of college of science ethics committee referenced by the number CSEC/0122/0036 in January 20, 2022. Blood samples were taken from each participant in the study and the serum was separated for determination the level of thyroid hormones (T4, T3 and TSH) by sandwich Enzyme-Linked Immunosorbent Assay (ELISA). The kits were products of PicoKine Company (USA). Also, the level of lipid profile include (TG, TC, HDL-C, LDL-C, and VLDL-C) were determined by spectrophotometrically. The kits were products of LiquiCHEK Company India. The statistical analysis system-SAS (2012) program was used to detect the effect of difference factors in study parameters. T-test used to compare the significant between means at probability level 0.01. The mean ± standard error (SE) was used to express all results (17).

Results and discussion

Age and BMI

The results of this study showed non-significant difference (*p>0.01*) in the age between the patients with hyperthyroidism (47.95 ± 1.76) years and controls (45.53 ± 2.04) years. On the other hand, there was highly significant (*p≤0.01*) decrease in the BMI of the patient with hyperthyroidism (22.74 ± 0.51 kg/m^2) in compared with healthy controls (25.06 ± 0.38 kg/m^2) as shown in table (1).

Table (1): Age and BMI values in hyperthyroid patients and control subjects. (Mean ± SE).

Group	Age (year)	BMI (kg/m^2)
Patients	47.95 ±1.76	22.74 ±0.51 b
Control	45.53 ±2.04	25.06 ±0.38 a
T-test	5716 .NS	1.304 **
P-value	0.885	0.0006
a-b different letters means….		

**** (*p≤0.01*), NS: Non-Significant.**

Other study showed that the prevalence of hyperthyroidism in the elderly is higher than in younger adults, with frequencies of about 3% in individuals older than 60 years of age(18). Witting *et al*. (19) confirmed the increasing prevalence of thyroid disorders with advancing age, but this is most pertinent with hyperthyroidism.

Consistent findings were reported by Vos *et al*. (20) who recorded an age mean of hyperthyroid patients equivalent to 30-50 years. While Piantanida *et al*. (21) found that the age mean of them was >20 years.

While the incidence statistics for overt hyperthyroidism in men and women from large population studies are analogous, at 0.4 per 1000 women and 0.1 per 1000 men, the age-specific incidence varies significantly (22).

Body mass index is another indicator biomarker for hyperthyroidism. The results showed that hyperthyroid patients are highly significant decrease in BMI in comparison with the control, and this result was in agreement with Torlinska *et al*. (23).Other studies agreed with the current study in that hyperthyroidism is a condition that occurs due to an exaggerate production of thyroid hormone by the thyroid (24,25). Another study showed that hyperthyroidism is the accompanied by multiple abnormalities with increased energy expenditure and excessive mobilization and utilization of metabolic substrates (26).

As well as the hyperthyroidism in aging individuals may be difficult to identification due to the confusing effect of drugs and acute or chronic diseases. Furthermore, in older patient with hyperthyroidism, there is a relative rarity of typical hyperadrenergic symptoms which may present with unexplained weight loss, cardiovascular effects or neuron cognitive changes (27).

Recent study demonstrated that the majority of patients with hyperthyroidism lose weight, but the effect is complex, and 10% of patients gain weight. Their treatment normally results in weight gain, and the study have shown that patients gain too much weight (28).

Peterson *et al*. (29) demonstrated that in human hyperthyroid patients, weight loss is associated with muscle wasting in hyperthyroid patients. Other study showed that hyperthyroidism is commonly associated with a variable loss in body weight due to a reduction in both lean and fat mass, as well as a

rise in overall energy expenditure, despite an increase in appetite (30). The latter occurs as a result of the biologic machine's reduced thermodynamic efficiency combined with increased heat output (31).

Level of thyroid hormone

Table (2) summarizes the results of the thyroid hormones levels in the patients with hyperthyroidism and control. There was a highly significant (*p≤0.01*) decrease in the level of TSH in patients with hyperthyroidism group (0.212 ± 0.01 µIU/ml) as compared with control group (2.319 ± 0.22 µIU/ml). Also there was a highly significant (*p≤0.01*) increase in the level of T3 in the patients with hyperthyroidism (3.662 ± 0.18 ng/ml) in comparison with the control group (1.482 ± 0.07 ng/ml). T4 estimation also showed highly significant (*p≤0.01*) increase in hyperthyroid patient (15.72 ± 0.50 µg/dl) when compared with control group (8.41 ± 0. 35 µg/dl).

Table (2): Thyroid hormones level in hyperthyroid patients and control subjects (mean ± SE).

Group	Hormone level		
	TSH (µIU/ml)	**T3 (ng/ml)**	**T4 (µg/dl)**
Patients	0.212 ±0.01 b	3.662 ±0.18 a	15.72 ±0.50 a
Control	2.319 ±0.22 a	1.482 ±0.07 b	8.41 ±0.35 b
T-test	0.317 **	0.528 **	1.512 **
P-value	0.0001	0.0001	0.0001
a-b different letters within column means…..			

**** (*p≤0.01*).**

The result of the study showed that patients with hyperthyroidism are highly significant increase in the T3 and T4 in comparison with the control on the other hand the hyperthyroid patients showed highly significant reduced in the TSH in comparison with the control and this result was agreement with Altaher *et al*. (26). Other study found that decreasing in TSH level in hyperthyroidism patients is in agreement with other researches that decreased TSH level and elevated thyroid hormones is an important marker in detecting thyrotoxicosis. Most cases of thyrotoxicosis are Graves` disease (GD) and toxic nodular goiter associated with hyperthyroidism (32).

A previous study done by Fadel *et al*. (33) on the initiation of hyperthyroidism is normally accompanied by a substantial decrease in TSH and a further increase in T3, T4 levels. This was consistent with current results.

The result of current study detected the increase production of T4 and T3 may be attributed to solitary or multiple thyroid nodules, which resulted because of hyperplasia of some follicular cells lead to increase iodide uptake more than surrounding tissues. Therefore elevated of T4 and T3 production, while TSH secretion is depressed the adjacent tissues in thyroid become inactive (34). TSH-receptor autoantibody (TRAb) formation causes hyperthyroidism by stimulating thyroid follicular cells, resulting in thyroid gland development and unregulated thyroid hormone synthesis and secretion (35). Other researcher showed a significant increase in T3 levels among hyperthyroidism as compared to controls. This may be due to increasing the level of iodine in the body by eating too much of iodine, inflammation of thyroid gland, too much synthetic thyroid hormone by the thyroid gland (36). T3 usually increases more than T4, probably because of increased

secretion of T3 as well as conversion of T4 to T3 in peripheral tissues. In some patients, only T3 is elevated (T3 toxicosis). T3 toxicosis may occur in any of the usual disorders that cause hyperthyroidism, including Graves' disease, multinodular goiter, and the autonomously functioning solitary thyroid nodule (37).

Lipid profile

Total cholesterol, LDL-C and HDL-C levels were highly significant (*p≤0.01*) decrease in patient with hyperthyroidism (147.49 ±1.60 mg/dl, 75.83 ±1.42 mg/dl and 42.87 ± 1.01 mg/dl) respectively in comparison with healthy control (192.78 ±2.05 mg/dl, 120.71 ±2.01 mg/dl and 59.01 ± 0.93 mg/dl) respectively.TG and VLDL-C levels showed highly significant (*p≤0.01*) increase in patient with hyperthyroidism (146.01 ±2.17 mg/dl and29.20 ± 0.43 mg/dl) respectively in comparison with healthy control (63.28 ±1.29 mg/dl and 12.65 ± 0.26 mg/dl) respectively as shown in table (3).

Table (3): Lipid profile in hyperthyroid patients and control subjects. (Mean ± SE).

Group	Lipid parameters (mg/dl)				
	Cholesterol	Triglyceride	HDL	LDL	VLDL
Patients	147.49 ±1.60 b	146.01 ±2.17 a	42.87 ±1.01 b	75.83 ±1.42 b	29.20 ±0.43 a
Control	192.78 ±2.05 a	63.28 ±1.29 b	59.01 ±0.93 a	120.71 ±2.01 a	12.65 ±0.26 b
T-test	6.204 **	6.387 **	3.144 **	6.001 **	1.275 **
P-value	0.0001	0.0001	0.0001	0.0001	0.0001

**** (*p≤0.01*).**

The results of the present study showed that total cholesterol, HDL-C and LDL were decreased in hyperthyroidism in comparison with control group. These results are agreed with Iqbal *et al.* (38).

Current study agrees with studies conducted by Rizos *et al*. (15) who found that hyperthyroidism is associated with decrease the level of total cholesterol, HDL-C, and LDL-C, while TGs is slightly increased. Present findings disagree with results obtained by Altaher *et al*. (26) who found that hyperthyroid did not affect lipid levels of patients in Saudi Arabia.

Hyperthyroidism is characterized by reduced serum TSH levels despite increased T4 and T3 levels. Altered lipid profile is a well-known manifestation of thyroid dysfunction. Both plasma LDL-C and HDL-C are increase in hypothyroidism while decrease in hyperthyroidism. Also, this agrees with current results (39).

Thyroid being a major endocrine gland with follicular cells (40) markedly affects lipid biosynthesis and its distribution. Lipids are organic compounds whose pivotal function is to provide energy. They are also main constituents of bio-membrane, providing vital precursor for important hormones (38).

In clinical hyperthyroid condition, there is an enhanced hepatic expression of LDL-C receptors, which in turn are regulated by the T3-mediated LDL receptor gene. Furthermore, LDL receptor's gene expression is also indirectly regulated by T3 via sterol regulatory element-binding protein-2(SREBP-2) (15). Overt hyperthyroid patients show reduced lipid levels. These observations have been shown to extend into the subclinical hypo/hyperthyroid range, suggesting that apart from thyroid hormones, thyroid-stimulating hormone (TSH) exerts independent effects on lipid metabolism. Recent advancement in molecular biology has enlightened us on the potential mechanisms of thyroid hormones and TSH in regulating lipid

metabolism (41). Thyroid hormones have been shown to induce the expressions of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, which is the initial reaction in cholesterol biosynthesis machinery. It has been observed that thyroid hormone increases the protein, mRNA, and functioning of HMG-CoA reductase (42, 43,44). Interestingly, hepatic lipogenesis is markedly amplified in hyperthyroid condition. This enhanced synthesis of lipids is also associated with increased lipolysis and its oxidation, thus, leading to their reduced levels in serum (45). It has been hypothesized that the low plasma cholesterol level of hyperthyroidism patients may be due to an increased clearance rate (26, 38).

Moreover, in many clinical situations, gradual reversal of hypocholesterolemia is considered a marker of reversal of critical illness and of patient recovery; likewise, severe persistent hypocholesterolemia, or further extreme drop in cholesterol, is a strongly unfavorable prognostic sign (46). It is worth mentioning here that decreased BMI observed in hyperthyroid condition can be an outcome of hypermetabolic condition and increased removal of lipids from the body. The levels of triglycerides were mildly elevated in both the subclinical and overt groups (47). This increasing trend can be explained from the fact that catabolism of triglycerides stored in adipose tissue is elevated by increased thyroid hormones; subsequently, it results in an increased concentration and turnover of nonesterified fatty acids (NEFA) (48). Lipid oxidation rate is enhanced that results in increased availability of fatty acids (30). Decrease in HDL-C levels is also observed in hyperthyroidism, due to increased CETP-mediated transfer of cholesteryl esters from HDL to VLDL and increased HL-mediated catabolism of HDL2 (15). Landázuri *et al*. (16) demonstrated that HDL subfractions are also affected by thyroid dysfunction; while the HDL2 subfraction was reduced in patients with hyperthyroidism, it was increased in patients with hypothyroidism. The treatment of both types of patients reversed these findings. It is believed that changes in HDL subfractions are mediated by the effect of thyroid hormone on hepatic lipase. In hyperthyroidism, the increase in LDL receptor mRNA leads to an increase in activity and number of LDL receptors this in turn, leads to a decrease in concentrations of LDL-C and TC levels. In another study, it is reported that hyperthyroidism induces a decrease in serum cholesterol, and this is agree with result of present study (39).

Conclusion

Our conclusions have been reached as a result of the current study that decrease of BMI in hyperthyroidism patients could be related with elevation of thyroid hormone. And the lipid profile was affected in hyperthyroid patients.

References

1. Kahaly, G. J.; Bartalena, L.; Hegedüs, L.; Leenhardt, L.; Poppe, K. and Pearce, S. H. (2018). European Thyroid Association guideline for the management of Graves'hyperthyroidism, European Thyroid journal, 7(4): 167-186.
2. Madariaga, A. G.; Santos, P. S.; Guillén-Grima, F. and Galofré, J. C. (2014). The incidence and prevalence of thyroid dysfunction in Europe: a meta-analysis. The Journal of Clinical Endocrinology and Metabolism, 99(3): 923-931.
3. Hollowell, J. G.; Staehling, N. W.; Flanders, W. D.; Hannon, W. H.; Gunter, E. W.; Spencer, C. A., *et al*. (2002). Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). The Journal of Clinical Endocrinology and Metabolism, 87(2): 489-499.
4. Douglas, S.; Ross, H. B. B.; David S.; Cooper, M.; Carol G.; Peter l., *et al*. (2016). American thyroid association guidelines for Diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. Thyroid 1343–1421. 26(10).
5. Zader, S. J.; Williams, E. and Buryk, M. A. (2019). Mental Health Conditions and Hyperthyroidism. Pediatrics, 144(5): e20182874.
6. Leo, M.; Bartalena, L.; Dottore, G. R.; Piantanida, E.; Premoli, P.; Ionni, I., *et al*. (2017).Effects of selenium on short-term control of hyperthyroidism due to graves' disease treated with methimazole: results of a randomized clinical trial. Journal of Endocrinological Investigation, 40(3): 281-287.
7. Palacios, S. S.; Pascual-Corrales, E. and Galofre, J. C. (2012). Management of subclinical hyperthyroidism. International Journal of Endocrinology and Metabolism. 10(2): 490-496.
8. LiVolsi, V. A. and Baloch, Z. W. (2018). The pathology of hyperthyroidism. Frontiers in Endocrinology, 9: 737.
9. Hu, S.; Ma, Q.; Li, B.; Wu, Q. and Han, R. (2020). Association of Hypothyroidism with Hypertensive Intracerebral Hemorrhage: A Case Control Study. World Neurosurgery, 134: 8-11.
10. Darras, V. M. (2022). Thyroid gland. In Sturkie's Avian Physiology pp. 795-812. Academic Press.
11. Bowden, S.A.; Goldis, M.; Congenital Hypothyroidism. (2021). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 –. PMID: 32644339.
12. Pirahanchi, Y.; Toro, F.; Jialal, I.; Physiology, Thyroid Stimulating Hormone. (2021). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 29763025.
13. Baliram, R.; Latif, R.; Zaidi, M. and Davies, T. F. (2017). Expanding the role of thyroid-stimulating hormone in skeletal physiology. Front. Endocrinology. (Lausanne). 8: 252.
14. Singh, G.; Gupta, V.; Sharma, A. K. and Gupta, N. (2011). Evaluation of thyroid dysfunction among type 2 diabetic Punjabi population. Advances in Bioresearch, 2(2): 3-9.
15. Rizos, C. V.; Elisaf, M. S. and Liberopoulos, E. N. (2011). Effects of thyroid dysfunction on lipid profile. The Open Cardiovascular Medicine Journal, 5: 76.
16. Landázuri, P.; Londoño-Franoo, Á. L.; Restrepo-Cortés, B. E.; Bayona-Zorro, A. L. and Sánchez-López, J. F. (2019). Dyslipidemia and its relationship with thyroid disease in farmers in the coffee-growing zone. Acta Medica Colombiana, 44(3): 8-15.
17. Timothy, A.; Carl, J.; Gregory, K. and Joyce, E. (2001). The jop satisfaction- jop performance relationship: a qualitative and qualitative review. Psychologichal Bulletin. 127(3): 376-407.
18. Mammen, J. S.; McGready, J.; Oxman, R.; Chia, C. W.; Ladenson, P. W. and Simonsick, E. M. (2015). Thyroid hormone therapy and risk of thyrotoxicosis in community-resident older adults: findings from the Baltimore longitudinal study of aging. Thyroid, 25(9): 979-986.
19. Witting, V.; Bergis, D.; Sadet, D. and Badenhoop, K. (2014). Thyroid disease in insulin-treated patients with type 2 diabetes: a retrospective study. Thyroid Research, 7(1): 1-6.
20. Vos, X. G.; Endert, E.; Zwinderman, A.; Tijssen, J. G. and Wiersinga, W. M. (2016). Predicting the risk of recurrence before the start of antithyroid drug therapy in patients with Graves' hyperthyroidism. The Journal of Clinical Endocrinology and Metabolism, 101(4): 1381-1389.
21. Piantanida, E.; Lai, A.; Sassi, L.; GallO, D.; Spreafico, E.; Tanda, M., *et al*. (2015).

Outcome prediction of treatment of Graves‘ hyperthyroidism with antithyroid drugs. Hormone and Metabolic Research, 47(10): 767-772.
22. Zimmermann, M. B. and Boelaert, K. (2015). Iodine deficiency and thyroid disorders. The Lancet Diabetes and Endocrinology, 3(4): 286-295.
23. Torlinska, B.; Nichols, L.; Mohammed, M. A.; McCabe, C. and Boelaert, K. (2019). Patients treated for hyperthyroidism are at increased risk of becoming obese: findings from a large prospective secondary care cohort. Thyroid, 29(10): 1380-1389.
24. De Leo, S.; Lee, S.Y. and Braverman, L.E. (2016). Hyperthyroidism. Lancet. 27: 388. 18.
25. Ferrari, S. M.; Ruffilli, I.; Elia, G.; Ragusa, F.,; Paparo, S. R.; Patrizio, A., *et al*. (2019). Chemokines in hyperthyroidism. Journal of Clinical and Translational Endocrinology, 16: 100196.
26. Altaher, W. H.; Ahemd, E. M. and Ismail, A. (2013). Assessment of lipids profile in hyperthyroidism Sudanese patients in North Kordofan State, Sudan. Natural and Medical Sciences (NMS) ,Vol. 14 version 1.
27. Samuels, M. H. (2018). Hyperthyroidism in Aging.In: Feingold KR, Anawalt B, Boyce A(eds). South Dartmouth (MA): MDText.com, Inc.
28. Kyriacou, A.; Kyriacou, A.; Makris, K. C.; Syed, A. A. and Perros, P. (2019). Weight gain following treatment of hyperthyroidism—A forgotten tale. Clinical obesity, 9(5): 12328.
29. Peterson, M.; Castellano, C. and Rishniw, M. (2016). Evaluation of body weight, body condition, and muscle condition in cats with hyperthyroidism. Journal of Veterinary Internal Medicine, 30(6): 1780-1789.
30. López, M.; Varela, L.; Vázquez, M. J.; Rodríguez-Cuenca, S.; González, C. R.; Velagapudi, V. R., *et al*. (2010). Hypothalamic AMPK and fatty acid metabolism mediate thyroid regulation of energy balance. Nature Medicine, 16(9): 1001-1008.
31. Silva, J. E. (2003). The thermogenic effect of thyroid hormone and its clinical implications. Annals of Internal Medicine, 139(3): 205-213.
32. Gilbert, J. (2017). Thyrotoxicosis–investigation and management. Clinical Medicine, 17(3): 274.
33. Fadel, B. M.; Ellahham, S.; Lindsay JR, J.; Ringel, M. D.; Wartofsky, L. and Burman, K. D. (2000). Hyperthyroid heart disease. Clinical Cardiology, 23(6): 402-408.
34. Baxter, J. D. and Webb, P. (2009). Thyroid hormone mimetics: potential applications in atherosclerosis, obesity and type 2 diabetes. Nat. Rev. Drug Discover. 8(4): 308.
35. Smith, T. J. and Hegedus, L. (2016). Graves‘ disease New England Journal of Medicine, 375(16): 1552-1565.
36. Kadiyala, R.; Peter, R. and Okosieme, O. (2010). Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. International Journal of Clinical Practice, 64(8): 1130-1139.
37. Benites-Zapata, V. A.; Urrunaga-Pastor, D.; Torres-Mallma, C.; Prado-Bravo, C.; Guarnizo-Poma, M. and Lázaro-Alcántara, H. (2017). Is free triiodothyronine important in the development of insulin resistance in healthy people?. Diabetes and Metabolic Syndrome: Clinical Research and Reviews, 11: 663-667.
38. Iqbal, M. A.; Ahmad, S.; Mumtaz, T.; Naseem, Z.; Malik, J.; Ahmad, H., *et al*. (2021). Prospective Analysis of Lipid Variations in Hyperthyroid Subjects from Lahore, Pakistan. BioMed Research International, 2021.
39. Jabuk, S. K.; Alta’ee, A. H. and Alterihy, F. A. (2012). The association between thyroid hormones and lipid profile in patients with primary hyperthyroidism. Medical Journal of Babylon, 9(4): 721-727.
40. Beserra, J. B.; Morais, J. B. S.; Severo, J. S.; Cruz, K. J. C.; de Oliveira, A. R. S.; Henriques, G. S., *et al*. (2021). Relation between zinc and thyroid hormones in humans: a systematic review. Biological Trace Element Research, 199(11): 4092-4100.
41. Chin, K. Y.; Ima-nirwana, S.; Mohamed, I. N.; Aminuddin, A.; Johari, M. H. and Ngah, W. Z. W. (2014). The relationships between thyroid hormones and thyroid-stimulating hormone with lipid profile in euthyroid men. International Journal of Medical Sciences, 11(4): 349.
42. Choi, J. W. and Choi, H. S. (2000). The regulatory effects of thyroid hormone on the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase. Endocrine Research, 26(1): 1-21.
43. Fawzi, S. M., Abdul-hassan, I. A., & Mahdi, B. M. (2018). Correlation between

thyroid hormones and anti-TSHR Ab in graves' disease. Iraqi Journal of Biotechnology, 17(1): 23-27.

44. Al-Shattawi, S. S., Al-Jumili, E. F., & Al-Azzam, M. A. (2018). The relationship between obesity and polycystic ovary syndrome in a sample of Iraqi infertile women. Iraqi Journal of Biotechnology, 17(3): 15-18.
45. Chen, Y.; Wu, X.; Wu, R.; Sun, X.; Yang, B.; Wang, Y., *et al*. (2016). Changes in profile of lipids and adipokines in patients with newly diagnosed hypothyroidism and hyperthyroidism. Scientific Reports, 6(1): 1-7.
46. Vyroubal, P.; Chiarla, C.; Giovannini, I.; Hyspler, R.; Ticha, A.; Hrnciarikova, D., *et al*. (2008). Hypocholesterolemia in clinically serious conditions--review. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub, 152(2): 181-189.
47. Iqbal, M. A. (2018). Predicitive biomarkers of cardiovascular risks in hyperthyroid patients from Lahore, Pakistan Doctoral dissertation, University of the Punjab, Lahore.
48. Beylot, M.; Martin, C.; Laville, M.; Riou, J. P.; Cohen, R. and Mornex, R. (1991). Lipolytic and ketogenic fluxes in human hyperthyroidism. The Journal of Clinical Endocrinology and Metabolism, 73(1): 42-49.
49. Kadhim, S. J., & Abdul-hassan, I. A. (2017). Correlation between vitamin D receptor gene polymorphisms and levels of some hormones in Iraqi infertile women with polycystic ovary syndrome. Iraqi Journal of Biotechnology, 16(4): 12-16.