Relation between Serum Lipids and Thyroid Hormones in Hypothyroidism Patients

Dheyaa Shinyar Hamad

Lecturer Community Health Technologies Department, Health and Medical Technologies College in Basrah, Southern Technical University, Iraq

Abstract

Background: Hypothyroidism is a condition that occurs as a result of a malfunction in the thyroid glands that leads to a decrease in the secretion of their main hormones. Thyroid hormones are known to be have an important role in the regulating metabolism of lipids; thus, any impaired in the thyroid function causes a significant change in the levels of lipid. **Objective:** To evaluate the changes occurs for lipid levels in hypothyroidism patients and determine the correlation between lipids parameters and some thyroid hormones. **Materials and Methods:** The study included 45 healthy control subjects and 52 hypothyroidism patients who visited private doctors' clinics in Basra, Iraq. Thyroid hormones and serum lipids were measured for both healthy subjects and hypothyroidism patients. **Results:** The study indicates an increase in the thyroid stimulating hormone (TSH) values for hypothyroidism patients as compared to the healthy control group while there is a slightly difference in the values of each of triiodothyronine (T_3) and thyroxine (T_4) between the two groups. There is a significant increase in the mean values of all lipids except for high density lipoprotein (HDL) in the hypothyroidism patients compared to that in healthy control subjects. The study presents that there is a positive correlation between TSH and all lipid parameters except for HDL which gives negative relation (r = - 0.20). There is a moderate correlation between TSH and non-HDL (r = 0.42) while the other lipids appear weak correlation (TC(r=0.14), TG (r=0.19). LDL (0.16), VLDL (0.17), and LDL/HDL (0.17)). There is no correlation between T_4 and TC (r = 0.03), LDL (r = 0.07). non-HDL (r = 0.04), and LDL/HDL (r = 0.06), HDL (r = - 0.02) while TG and VLDL appears weak correlation (r = - 0.11 to each one of them). **Conclusions:** The study found that the abnormal change in the levels of lipids during hypothyroidism may increase the likelihood for occurrence of arteriosclerosis and the emergence of cardiovascular disease in hypothyroidism patients. There is a moderate positive relationship between TSH and non-HDL levels, as this indicates that non-HDL should be added to lipid profile tests as evidence of measuring cardiac risk in patients with hypothyroidism.

Keywords*: hypothyroidism, atherosclerosis, T_4, TSH, non-HDL.*

Introduction

The thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4) are synthesized by the follicular epithelial cells of the thyroid gland by utilizing from dietary iodine [(1)]. Thyroid gland secretesT_3 and T_4hormones into the bloodstream, these hormones have vitally important to the body's metabolism and normal development [(2)].

Corresponding author:
Dheyaa Shinyar Hamad
E-mail: dhyashinyar1@gmail.com
(Tel.07703132455)

The synthesis and secretion of thyroid hormones is controlled by hypothalamic-pituitary-thyroid axis [(3)]. The hypothalamus secretes thyrotropin-releasing hormone (TRH) which alerts the thyrotrope cells in the anterior pituitary gland to secrete the thyroid-stimulating hormone (TSH), this hormone stimulates the thyroid cells to produce and secretetheT_3 and T_4 hormones [(4)].

Thyroid hormones enter the cells through specific energy-dependent carriers [(5)]. Inside the cell, T_4 is metabolized to T_3, which then bind to its nuclear receptors in the target cells, which in turn activate T_3-responsive genes. These genes modify many of

cell functions including the metabolism of lipids, carbohydrates and proteins [6, 7].

Hypothyroidism is the most common condition in the thyroid diseases, it results from any condition that leads to a decrease in the production of hormones T_3 and T_4. Hypothyroidism is associated with an abnormal lipids metabolism that may cause atherosclerosis and then lead to a cardiovascular disease [8].

Laboratory diagnosis of hypothyroidism is mostly done by measuring TSH and T_4 levels in the blood. A lower T_4 levels and increased TSH levels indicate primary hypothyroidism. This happens when the pituitary gland realize that the thyroid gland doesn't make enough hormones so it releases more TSH in an attempt to stimulate the thyroid gland to produce their hormones. But if the thyroid gland is not working properly, it will not interact with the pituitary gland signals this leads to high levels of TSH and low levels of T_4 [9, 10].

Thyroid hormones have an important role to maintain the normal cholesterol levels in the blood needed to meet the body's natural requirements [11]. Thyroid hormones regulate serum cholesterol levels through controlling many of its metabolic pathways like; stimulating vital cholesterol synthesis and export it, the processes of reverse transport of cholesterol from the peripheral tissues to the liver, activity of the receptors present in the liver cells that responsible on converting the cholesterol into bile [12].

Hypothyroidism is a known cause of hyperlipidemia. the most common lipid abnormality in hypothyroidism patients is high cholesterol in the blood, most often the low-density lipoproteins (LDL), because it is the main lipoprotein responsible for transporting cholesterol from the liver to the cells of the body. Also, increase in plasma triglycerides (TG) may occurs due to an increased in the esterification of fatty acids in the liver [13].

The value of non-high-density lipoprotein (non-HDL) has emerged as an indicator of cardiovascular disease recently. its value represents the sum of the cholesterol accumulated in all lipoproteins, with the exception of HDL, such as: chylomicrons, VLDL, LDL and Lp (a) so it reflects the full effect of all blood lipid components that are involved in atherosclerosis [14].

The current study done to determine the association between thyroid hormones and serum lipids in hypothyroidism patients and to determine which one of lipids affected more by these hormones.

Material & Method

The study was conducted on fifty-two untreated hypothyroidism patients who visited private doctors' clinics in Basra, Iraq in the period from May to December, 2019. Also, forty-five normal healthy subjects were included as controls.

Blood samples were drawn after an overnight fast and separated into a serum. Then the serum samples were analyzed for study parameters.

The serum levels for TC, TG, and HDL were measured by enzymatic colorimetric assay method using a randox kits. VLDL and LDL were calculated using the Friedewald formula [15]. The levels for non-HDL-C were calculated mathematically by subtracting HDL value from TC value (TC – HDL).

Serum concentration of T_3, T_4 and TSH were measured by micro plate competitive enzyme immunoassay on the TOSOH system analyzers.

The results were calculated as mean±SD, then was analyzed statistically by using SPSS program to find if there is a significantly change in the parameters levels between patients and control groups. p values which were less than or equal to 0.05 were considered to be statistically significant [16].

Results

Table 1. demonstrates the values of mean ± SD of thyroid hormones in both hypothyroidism and control groups. There is a significant increase in the mean values of TSH in the hypothyroidism patients' group when compared to that of healthy control group ($p < 0.0001$) while there is no significant difference in the mean values of both T_3 and T_4 between these two groups ($p = 0.26$ and $p = 0.12$ respectively).

Table 2. demonstrates the values of mean ± SD for all lipid parameters in both hypothyroidism patients and healthy control groups. Comparing the levels of means between hypothyroidism patients and healthy control groups, we note that there is a high significant increase

in the mean values of all lipids (P < 0.0001), with the exception of HDL showing a significant decrease in mean values (P < 0.0001).

Table 3 appears that there is a positive correlation between TSH and all lipid parameters except for HDL which gives negatively relation (r = - 0.20). There is a moderate correlation between TSH and non-HDL (r = 0.42) while the other lipids appear weak correlation (TC (r= 0.14), TG (r= 0.19), LDL (0.16), VLDL (0.17), and LDL/HDL (0.17)).

Table1: comparison of thyroid hormones levels between hypothyroidism patients and healthy control groups

Parameters	Hypothyroidism patients	Healthy control	P value
T3 (ng/ml)	1.94 ± 0.18	1.25±0.30	0.26
T4 (µg/dl)	6.35 ± 1.61	6.92±1.79	0.12
TSH (µIU/L)	11.75 ± 2.65	1.93±0.24	0.0001

All values are given in mean ± standard deviation (SD)

Table 2: Comparison of lipid parameters levels between hypothyroidism patients and healthy control groups

Lipid Parameters (mg/dl)	Hypothyroidism Patients	Healthy control	P value
TC	210.57±9.90	169.29±13.07	0.0001
HDL	28.78±3.70	40.17±3.18	0.0001
LDL	144.88±12.02	107.71±13.70	0.0001
TG	193.48±14.02	107.48±9.04	0.0001
VLDL	38.69±2.79	21.40±1.83	0.0001
Non-HDL	178.15±12.97	129.11±13.33	0.0001
LDL/HDL	5.12±1.00	2.69±0.42	0.0001

All values are given in mean ± standard deviation (SD)

Table 3: Correlation coefficient (r) between TSH And lipids in hypothyroidism patients

Parameter	Correlation coefficient (r)
TSH & TC	0.14
TSH & TG	0.19
TSH & LDL	0.16
TSH & HDL	- 0.20
TSH & non-HDL	0.42
TSH & VLDL	0.17
TSH & LDL/HDL	0.17

Table 4 appears no correlation between T_4 and each of TC (r = 0.03), LDL (r = 0.07). non-HDL (r = 0.04), and LDL/HDL (r = 0.06), HDL (r = - 0.02) while TG and VLDL appears weak correlation (r = - 0.11 to each one of them).

Table 4: Correlation coefficient (r) between T_4 and lipids in hypothyroidism patients

Parameter	Correlation coefficient (r)
T4 & TC	0.03
T4 & TG	- 0.11
T4 & LDL	0.07
T4 & HDL	- 0.02
T4 & non-HDL	0.04
T4 & VLDL	- 0.11
T4 & LDL/HDL	0.06

Fig. 1 shows the only negative correlation between TSH and lipids and that occurs only between TSH and HDL.

Fig. 2 shows the only moderate correlation between TSH and lipids that occurs only between TSH and non-HDL.

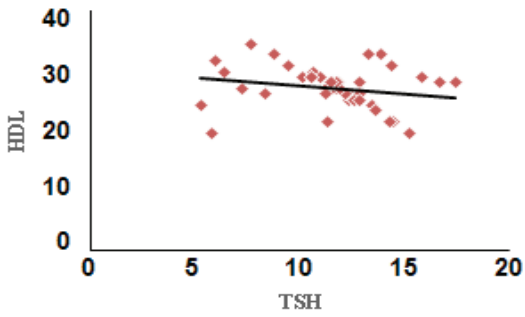

Fig. 1: correlation between TSH and HDL

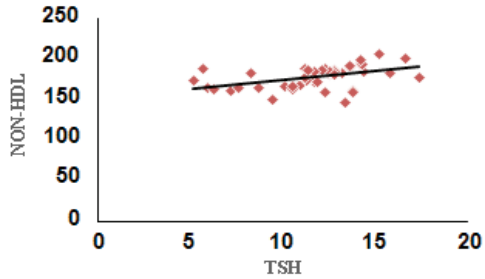

Fig. 2: correlation between TSH and non-HDL

Discussion

The study indicates an increase in all serum lipids values except for the HDL in the hypothyroidism patients compared to that in healthy control subjects. Other researchers have proven the same results that obtained in our research [17, 18, 19].

Hydroxy methyl glutaryal reductase (HMGCR) is the major enzyme responsible for regulating the cholesterol synthesis in the liver [20].

There are several mechanisms interprets how the activity of HMGCR regulated, one of which is through a balance between the phosphorescent and non-phosphorous forms in which the enzyme is exists. It has been observed that an increase in the non-phosphorous form increases the activity of the enzyme, while the increase in its phosphorous form reduces its activity [21,22].

Special kinase enzyme, AMP-activated protein kinase (AMPK) is responsible for the interconversion between the phosphorescent and non-phosphorous forms of HCGM enzyme [23].

Subclinical hypothyroidism characterized by a rise in the serum TSH levels with normal values for both T_3 and T_4. Several studies indicate that high TSH levels in hypothyroidism cause inhibition to the AMPK activation in the

liver which make activation for HMGCR by increasing its dephosphorylation form and this in turn stimulate the synthesis of cholesterol and increase its serum levels [24, 25].

The most common explanation for increased LDL levels in patients with hypothyroidism is the effect of thyroid hormones on LDL receptors, as these hormones

works to lower the ratio of these receptors which leads to a decrease in the clearance of LDL from the bloodstream [26].

The rise in the serum TG in hypothyroidism patients may be due to the effect of thyroid hormones on lipoprotein lipase enzyme, which cause decrease in its efficacy and this works to reduced clearance of TG from its rich lipoproteins and hence elevated in the serum TG levels occurs [27, 28].

The thyroid hormones effects on the HDL metabolism is through the activities of cholesterol transport protein (CETP) and hepatic lipase (HL) enzymes associated with HDL metabolism. CETP is responsible for transporting cholesterol esters from HDL_2 to VLDL and IDL and backward transfer for TG into HDL_2. TG is then hydrolyzed by HL into fatty acids, at this point HDL_2 changes to be HDL_3. Thus, HL is the enzyme responsible for lipid analysis by converting IDL to LDL and HDL_2 to HDL_3 [29, 30].

Correlation analysis for our study showed a moderate positive relationship between the levels of TSH and non-HDL in hypothyroidism patients' group. This finding is consistent with the results of other studies [31, 32].

The non-HDL test can be considered as an important indicator of cardiovascular disease because its value expresses the total number of the cholesterol present in all particles that causes atherosclerosis [33].

Conclusion

The results of our research indicated that hypothyroidism has a significant impact on blood lipid levels, especially those responsible on causing atherosclerosis that leading to vascular heart disease. Considering a non-HDL test as a primary goal for measuring dyslipidemia with other lipid parameters as a useful indicator for measuring heart risks in patients with hypothyroidism.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Obtain from college

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