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Study to the effect of Thyroid Dysfunction on Lipid Profile

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Abstract:

This study was carried out to investigate the pattern of lipid profile in individuals with thyroid dysfunction and healthy control and to know whether any correlation exists between serum lipids and thyroid hormones.

The study was performed on 125 persons, among them 73 had thyroid dysfunction were accepted in the study as patients group and 52 subjects with normal thyroid function and no history of chronic diseases were taken as control group. Then the patient group subdivided into hypothyroidism and hyperthyroidism groups on the bases of clinical examination and laboratory investigation for thyroid hormones. Serum total cholesterol (TC), High density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C), very low density lipoprotein (VLDL), and Triglyceride (TG) were assessed in all groups.

Our study indicate that there is a highly significant increase ($p<0.0001$) in the levels of TC, LDL, VLDL, and TG whereas HDL levels was found significantly decreased in hypothyroidism cases compared to hyperthyroidism and control subjects. Hyperthyroidism patients present highly significant decrease in serum level of TC, TG, LDL, and VLDL ($p<0.0001$) compared to control subjects. There is significantly increase in the activity of HDL in hyperthyroidism patients when compared with control subjects ($p<0.001$). I conclude that any increase in the levels of lipid fractions LDL, TC, VLDL and TG with a decrease in HDL levels may be contributory factor to the

high risk of atherosclerosis induced coronary heart disease observed in hypothyroidism patients.

Key words: Hypothyroidism, Hyperthyroidism, thyroid hormone, lipid profile, atherosclerosis

INTRODUCTION

The main function of thyroid gland is the production and secretion two types of hormones, thyroid hormone and calcitonin. Calcitonin is the calcium regulating hormone. Thyroid hormone has a role in the regulation of body metabolism, neurological development, and other body functions. There are two metabolically active forms of thyroid hormone, triiodothyronine (T_3) and tetraiodothyronine (T_4) which also called thyroxine [1, 2].

Thyroid hormone production is regulated by a hypothalamic-pituitary-thyroid system. The hypothalamus gland synthesizes and stores the thyrotropin-releasing hormone (TRH). Secretion of this hormone stimulate the pituitary gland to release the thyrotropin stimulating hormone (TSH), which is in turn circulates to thyroid gland and stimulate it to produce and release of thyroid hormone [3, 4].

The most common presenting clinical features of thyroid disease are the result of; hypothyroidism, due to decrease thyroid hormone secretion, with a normal or high TSH, or hyperthyroidism, due to excess thyroid hormone secretion with low TSH [5]. Clinically, individuals with hyperthyroidism will have symptoms of increased metabolism such as appetite change, tachycardia and fatigue, while individuals with hypothyroidism have symptoms of lowered metabolism like edema, dry skin and constipation [6, 7].

Thyroid function regulates a wide array of metabolic parameters; they affect synthesis, mobilization and degradation of lipids. Thyroid hormone increases cholesterol synthesis in

the liver and increases its conversion to bile salts. The thyroid hormone, T_3 has the ability to sensitize the adipocyte to the lipolytic action of epinephrine this increases the flow of fatty acids to the liver and thereby indirectly increases hepatic triacylglycerol synthesis [8].

Lipid profile is a group of blood tests that are often ordered together to determine risk of cardiovascular disease (CVD). It includes total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), and triglyceride (TG) [9]. Lipids are hydrophobic, means insoluble in water this make them to be cannot transport in the blood by themselves, so it binds to protein and form lipoproteins to transport fats such as cholesterol, phospholipids, and triglycerides around the body. LDL frequently labeled as being bad cholesterol because it transport fat to the artery walls which in turn can lead to atherosclerosis. HDL carries cholesterol and other fats away from the artery walls to the liver, and because a higher level of HDL is associated with a decreased risk of atherosclerosis it is known as the good cholesterol. VLDL transport fats and cholesterol into the bloodstream. When compared to the other types of lipoproteins, VLDL contains the highest amount of triglycerides, and it is considered to be a bad type of cholesterol [10, 11].

Thyroid hormones regulate lipoprotein metabolism, whereas thyroid diseases considerably alter lipid profile. However studies have shown that lipid profile in subjects with thyroid dysfunction varies among individuals and in different countries [12, 13, 14].

The present study is designed to study the pattern of lipid profile in individuals with thyroid dysfunction and healthy control and to know whether any correlation exists between serum lipids and thyroid hormones.

MATERIALS AND METHODS

The study was carried out during the period from November 2016 to June 2017 on 125 subjects visiting the General Qurna hospital, from Basra, Southern of Iraq with suspicion of thyroid disorders, among them seventy three had thyroid dysfunction were accepted in the study as patients cases. Fifty two subjects with normal thyroid function and no history of chronic diseases were taken as control group. Detailed information of all subjects was collected that included age, sex and family or personal history of chronic diseases. Then the patient cases subdivided into hypothyroidism and hyperthyroidism groups on the bases of clinical examination and laboratory investigation.

Venous samples were drawn after 12 hours of overnight fasting. Serum was separated and assays were performed within 24 hrs. Serum T_3, T_4 and TSH were measured by micro plate competitive enzyme immunoassay on the TOSOH analyzers. Serum total cholesterol (TC) and triglyceride (TG) were determined by enzymatic colorimetric assay using the kit from Biolabo, France depending on CHOD-PAP and GPO methods respectively. High density lipoprotein (HDL) was determined enzymatically in the supernatant after Phosphotungstate method precipitation of other lipoproteins using the kit from Randox, United Kingdom. Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) was calculated using the Friedewald formula [15].

Statistical analyses were performed by using SPSS for Windows version 16.0. Data were expressed as the mean ± SD. The comparisons between groups were performed with analysis of variance (ANOVA). Confidence limits equal or higher than 95% were considered to be statically significant $p<0.05$, while confidence limits equal or higher than 99% were considered to be statically highly significant $p<0.01$ [16].

RESULTS

The mean levels for T_3, T_4, and TSH hormones in hypothyroidism, hyperthyroidism, and control subjects are shown in table 1 and figure 1.

Hypothyroidism patients had highly significant increase in TSH levels ($p<0.0001$) as compared with hyperthyroidism patients and control subjects. There was a highly significant decrease in TSH levels ($p<0.001$) in hyperthyroidism patients as compared with control subjects.

Hypothyroidism patients had highly significantly decrease in the levels of T_3 and T_4 as compared with hyperthyroidism patients and control subjects ($p<0.0001$ and $p<0.001$ respectively). There was also a highly significant increase in T_3 and T_4 ($p<0.0001$) in hyperthyroidism patients as compared with control subjects.

Table 1 showing mean±SD of T_3, T_4, and TSH of thyroid dysfunction and control subjects

	Hypothyroidism	Hyperthyroidism	Control
TSH	***a ***b 11.655±1.266	**a 0.825±0.343	1.189±0.114
T_3	**a ***b 0.806±0.262	***a 4.405±0.714	1.028±0.693
T_4	**a ***b 5.496±0.828	***a 11.765±1.965	6.496±0.686

a hypothyroidism and hyperthyroidism significant compared to control group (**p < 0.001, ***p < 0.0001)

b hypothyroidism significant compared to hyperthyroidism group (**p < 0.001, ***p < 0.0001).

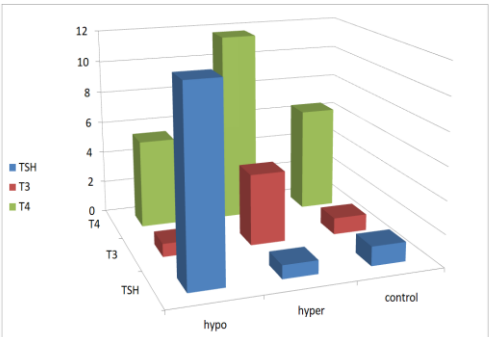

figure 1: Distribution of thyroid hormone levels in all study groups

Table 2 and figure 2 demonstrates the mean levels of lipid profile activity in all study groups.

Hypothyroidism patients present an abnormal lipid profile with highly significant increase in the levels of TC, TG, LDL, and VLDL ($p<0.0001$) compared to hyperthyroidism patients and control subjects. There is a highly significant decrease in the activity of HDL in hypothyroidism patients when compared with hyperthyroidism patients ($p<0.001$), but there is a significantly increase in the activity of HDL in hypothyroidism patients when compared with control subjects ($p<0.001$).

Hyperthyroidism patients present a highly significant decrease in the levels of TC, TG, LDL, and VLDL ($p<0.0001$) compared to control subjects but within the normal values. There is a highly significant increase in the activity of HDL in hyperthyroidism patients when compared control subjects ($p<0.0001$).

Table 2. Comparison of lipid profile fractions between all study groups

All values are given in mean±SD

	Hypothyroidism	Hyperthyroidism	Control
TC	***a ***b 280.295±39.656	***a 162.942±8.701	178.590±8.161
TG	***a ***b 202.051±26.823	***a 112.422±12.916	125.484±7.401
HDL	**a **b 36.068±5.183	***a 39.653±5.361	33.787±3.747
LDL	***a ***b 202.637±35.296	***a 99.769±12.425	120.196±6.486
VLDL	***a ***b 40.362±5.270	***a 22.707±3.055	25.109±1.44

a hypothyroidism and hyperthyroidism significant compared to control group (**p < 0.001, ***p < 0.0001)

b hypothyroidism significant compared to hyperthyroidism group (**p < 0.001, ***p < 0.0001).

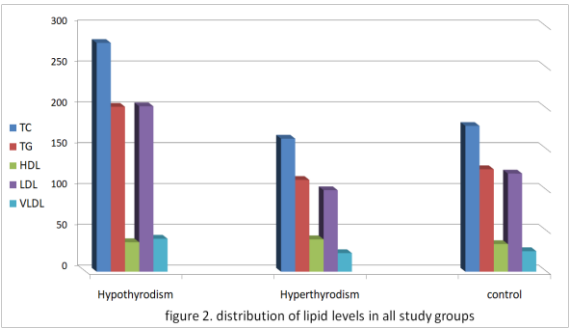

figure 2. distribution of lipid levels in all study groups

DISCUSSION

In our study, the mean total cholesterol, LDL-C, VLDL and TG were found significantly increased, whereas HDL-C was found significantly decreased in hypothyroidism cases compared to hyperthyroidism and control subjects; this showed that hypothyroid patients present a high risk for atherosclerosis and secondary dyslipidemia, which may represent an increased risk

for coronary heart disease. These data agree with other studies [17, 18, 19].

Regulation of TC and LDL levels can be attributed to altered clearance of LDL-C from plasma by changes in the number of LDL receptors on liver cell surfaces [20, 21].The promoter of the LDL receptor gene contains a thyroid hormone responsive element (TRE), T_3 bind directly to TRE and modulate the gene expression of LDL receptor [22]. Moreover thyroid hormones stimulate the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, enzyme catalyzed the first step in cholesterol biosynthesis [23]. On the other hand the effect of thyroid hormone on cholesterol 7-α-hydroxylase (CYP7A), this enzyme catalyzes the rate-limiting step for the synthesis of bile acid from cholesterol. CYP7A is regulated by T_3 then in hyperthyroid conditions more cholesterol is converted to bile acids, which are excreted in the feces this make serum cholesterol levels decline [24, 25].

Regulation of TG levels can be attributed to alter clearance of TG from plasma by changes the activity of lipoprotein lipase (LPL) by thyroid hormone. The enzyme LPL is synthesized and secreted by adipocyte, and is important for the transfer of triacylglycerol fatty acids from the circulating blood into adipocyte [26]. Moreover, a decrease in LPL activity is found in hypothyroidism, decreasing the clearance of TG by adipocyte lead to increase TG levels in plasma and this associated with increased levels of VLDL [27, 28].

Our study also show decreasing in HDL levels in hypothyroidism patients mainly due to the regulation of cholesterol ester transfer protein (CETP) and hepatic lipase (HL) activity by thyroid hormone [29, 30].

The cholesterol taken up by HDL is esterified then either taken up by the hepatic scavenger receptor class B type I (SRBI), or transferred to apoB-containing lipoproteins in exchange for triglycerides by CETP [31].

Hepatic lipase is a lipolytic enzyme hydrolyzes triglyceride and phospholipid in HDL and also stimulates HDL cholesterol ester uptake by hepatocyte. Therefore, hepatic lipase, together with lipid transfer proteins, determines both HDL level and its function in reverse cholesterol transport [32].

The present study shows that there is inverse relationship between serum thyroid hormone and serum lipid levels (except HDL). Monitoring of lipid profile is necessary for subjects suffering from thyroid dysfunction to anticipate any cardiac risk.

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