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A STUDY OF LIPID PROFILE IN HYPERTHYROIDSM PATIENTS

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Abstract: Thyroid hormones are important at cellular level, affecting nearly every type of tissue in the body. **Objectives:** The present study was carried out to determine whether thyroid hormones affect lipid profile in patients with hyperthyroidism. **Materials and Methods:** This study was carried out on 20 hyperthyroid patients (10 men and 10 women) with mean age 48.5+13.1 years and 22 apparently healthy controls (11 men and 11 women) with mean age 49.5+11.4 years. Serum levels of thyroid stimulated hormone TSH, thyroxine (T4) and triidothyronine (T3) were measured by Qualigens ELISA Plate reader and washer, and total cholesterol (TC), high –density lipo-protein cholesterol (HDL-C), and Triglyceride (TG) were measured by Semi Auto analyzer RA - 50, while low-density lipoprotein cholesterol (LDL-C) and low-density lipoprotein cholesterol (VLDL-C) were calculated. **Results:** Thyroid stimulated hormone TSH, lipids and lipoproteins (TC, TG, HDL-C, LDL-C, VLDL-C) levels of patients were significantly lower than those of the control group ($p>0.05$).And there were significant increases in serum thyroid hormones T4, T3 values ($p>0.05$). **Conclusion:** Hyperthyroidism is associated with decrease levels of lipoprotein, caused by increased hepatic uptake due to enhanced affinity for the LDL receptor, and regulatory protein of TG (ApoAV).

Keywords: T3, T4, TSH, Cholesterol, HDL-C, LDL-C, VLDL-C

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INTRODUCTION

Thyroid disease, namely hypothyroidism and hyperthyroidism, constitutes the most common endocrine abnormality in recent years, diagnosed either in subclinical or clinical form. According to the 6-year duration (National Health and Nutrition Examination Survey III (NHANES) III Study 1988-1994, the prevalence of hyperthyroidism 1.3% (0.5% clinical and 0.7% subclinical), in population aged at least 12 years, showing an age and sex dependence [1]. Thyroid disease is associated with various metabolic abnormalities, due to the effects of thyroid hormones on nearly all major metabolic pathways. Thyroid hormones regulate the basal energy expenditure through their effect on protein, carbohydrate, and lipid metabolism. This might be a direct effect or an indirect effect by modification of other regulatory hormones such as insulin or catecholamine [2].

Dyslipidemia is a common metabolic abnormality in patients with thyroid disease, either in the overt or subclinical forms of the disease, and constitutes the end result of the effect of thyroid hormones in all aspects of lipid metabolism leading to various quantitative and/or qualitative changes of triglycerides, phospholipids, cholesterol, and other lipoproteins [3].

In thyroid disease, dyslipidemia and the coexisting metabolic abnormalities, in combination with the thyroid hormone-induced hemodynamic alterations, explain the high risk for cardiovascular disease [4- 6].

It is well established that overt hyperthyroidism induces a hyperdynamic cardiovascular state (high cardiac output with low systemic vascular resistance), which is associated with a faster heart rate, enhanced left ventricular systolic and diastolic function, and increased prevalence of supraventricular tachyarrhythmia's [7].

Although thyroid hormones play an important role in cardiovascular hemodynamics, the association between elevated thyroid hormones and low grade inflammation is still unclear [8].

Thyroid gland function regulates a wide range of metabolic events. Thyroid gland function significantly affects lipoprotein metabolism and as a result the cardiovascular disease (CVD) risk [9, 10]. In fact, even within the normal range of thyroid-stimulating hormone (TSH) values, a gradual elevations in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) and a linear depletion in high-density lipoprotein cholesterol (HDL-C) levels has been observed with increasing TSH [11,12].

In healthy people, the thyroid makes just the right amounts of two hormones, thyroxine (T4) and triiodothyronine (T3), which have important actions throughout the body. These hormones regulate many aspects of our metabolism, eventually affecting how many calories we burn, how warm we feel, and how much we weigh. These hormones also have direct effects on most

organs, including the heart, which beats faster and harder under the influence of thyroid hormones. Essentially, all cells in the body will respond to increases in thyroid hormone with an increase in the rate at which they conduct their business [13].

Determination of the serum TSH is the most sensitive way to screen for hyperthyroidism. A marked improvement in the sensitivity of the TSH assay makes it possible to diagnose hyperthyroidism solely on the basis of an absence of detectable TSH. Most patients with overt hyperthyroidism have TSH levels of less than 0.05 µU/mL. As long as the hypothalamic–pituitary axis is intact, an absence of detectible TSH represents the appropriate response to too much circulating thyroid hormone.

Undetectable TSH by second- or third-generation assay is diagnostic of hyperthyroidism. A normal TSH level virtually rules out hyperthyroidism, unless a rare TSH-secreting pituitary adenoma is present [14].

MATERIALS AND METHODS

This study was carried out on 22 hyperthyroid subjects (11 men and 11 women) (mean age 48.5±13.1 years) whom were collected from Government General Hospital , Rajiv Gadhi Institute of Medical Sciences, Ongole between 2009-2010. The diagnosis of hyperthyroidism was made on the basis of clinical examination, elevated circulating levels of (T4) or (T3) and suppressed TSH levels. The causes of hyperthyroidism were Graves disease in all of the patients.

The control group includes 24 apparently healthy individuals (12 men and 12 women) (mean age 47.5±11.4 years), after having been asked about their health.

Fasting blood samples to determine the thyroid function TSH, T4, T3, TC, TG and HDL-C were drawn at beginning of the study and LDL-C and VLDL-C was calculated.

Levels of total cholesterol, triglyceride and HDL-C were measured by Semi Auto analyzer RA – 50, Autopak kits supplied by BAYER Diagnostics India Ltd are used. While the TSH, T4 and T3 were measured by Qualigens ELISA plate reader and washer supplied by Amar Immunodiagnostics Pvt Ltd.

Statistical analysis

This study is a case-control study. Student's t-test has been used to determine the significant difference between two groups, where p values of less than 0.05 is considered significant.

RESULTS

The concentrations of serum thyroid hormones (T3 and T4), lipids (cholesterol and triglyceride), lipoproteins (HDL-cholesterol, LDL-cholesterol and VLDL-cholesterol) and TSH in patient with hyperthyroidism are presented in Table 1. There were significant increases (p> 0.05) in serum thyroid hormones (T4 ,T3) values, and also the table show as there were a significant decreases in TSH, lipids and lipoproteins (TC, TG , HDL-C, LDL-C,VLDL-C) values (p> 0.05) in patient group than control group.

Table 1 Lipid profile and thyroid hormones values in control and patients.

Parameter		Control	Patient	*P-Value*
		Mean ± SD	Mean ± SD	
TSH	(µlU/ml)	1.34 ± 0.5	0.5 ± 0.4	0.00
T4	(µg/dl)	6.97 ± 1.8	9.65 ± 3.76	0.00
T3	(ng/ml)	0.50 ± 0.211	2.1 ± 0.87	0.00
T4/T3	ratio	14.32 ± 8.53	4.59 ± 4.32	0.00
TC	(mg/dl)	238.5 ± 28	200 ± 53.9	0.03
TG	(mg/dl)	184.5 ± 28.4	157.5 ± 28.8	0.02
HDL-C	(mg/dl)	41.9 ± 0.7	32 ± 5.8	0.04
LDL-C	(mg/dl)	159 ± 28	104.5 ± 52.1	0.00
VLDL-C	(mg/dl)	34.9 ± 5.68	31.5 ± 5.76	0.02

DISCUSSION

Thyroid function regulates a wide array of metabolic parameters. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors [9][10]. Indeed, in the case of high level range of thyroid-stimulating hormone (TSH) values, there are a linear increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) and there are a linear decrease in high-density lipoprotein cholesterol (HDL-C) and this agree with our result [11].

Thyroid hormones induce the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, which is the first step in cholesterol biosynthesis. Moreover, triiodothyronine (T3) upregulates LDL receptors by controlling the LDL receptor gene activation. This T3-mediated gene activation is done by the direct binding of T3 to specific thyroid hormone responsive elements (TREs) [15]. Furthermore, T3 controls the sterol regulatory element-binding protein-2 (SREBP-2), which in turn regulates LDL receptor's gene expression [16]. T3 has also been associated with protecting LDL from oxidation [17]. This may explain the results of present study.

Thyroid hormones can influence HDL metabolism by increasing cholesteryl ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL2 to the very low density lipoproteins (VLDL) and TGs to the opposite direction [18]. In addition, thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the TG-rich lipoproteins, and the hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 and contributes to the conversion of intermediate-density lipoproteins (IDL) to LDL and in turn LDL to small dense LDL (sdLDL) [19][20]. Another effect of T3 is the up-regulation of apolipoprotein AV (ApoAV), which plays a major role in TG regulation [21]. Indeed, increased levels of ApoAV have been associated with decreased levels of TGs [22]. Proposed mechanisms for this effect include the decrease of hepatic VLDL-TG production and the increase of plasma LPL levels and activity, resulting in increase of lipoprotein generation due to enhanced LPL-mediated lipolysis of VLDL-TG [22]. Moreover, a greater clearance of lipoprotein, caused by increased hepatic uptake due to an enhanced affinity for the LDL receptor, has also been ascribed to ApoAV [22]. This might be explain the decrease in VLDL-C and TG in the present study

Hyperthyroidism has profound effects on cardiovascular system, including reduced systemic vascular resistance due to relaxation of vascular smooth muscle cells, enhanced heart rate and cardiac output due to increase in cardiac diastolic relaxation, contractility and heart rate [23]. Hyperthyroidism is characterized by reduced serum TSH levels despite increased thyroxine (T4) and triiodothyronine (T3) levels.

Altered lipid profile is a well-known manifestation of thyroid dysfunction. Both plasma LDL-C and HDL-C increase in hypothyroidism and de-crease in hyperthyroidism [24-28]. Also, this agrees with our results.

It is well-known that thyroid dysfunctions have profound effects on lipoprotein metabolism [29]. The main cause of the differences in total cholesterol concentrations is the alterations of LDL-C levels. In hyperthyroidism, the increase in LDL receptor mRNA leads to an increase in activity and number of LDL receptors [30]. 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 [31], and this is agree with result of present study.

In hyperthyroid cases a decrease in HDL-C levels are also observed [32]. This decrease suggested being due to increased hepatic triglyceride lipase activity. Through the effects of thyroid hormones, hepatic lipase, a decrease, in HDL2/ HDL3 is reported. The most prominent alteration in HDL-C is due to the changes in HDL2 sub-fraction [29]. These findings are consistent with the literature [33].

It is important to achieve an euthyroid state as soon as possible in hyperthyroid patients. However, normalization of hyperthyroid hormones is frequently associated with the elevation of proatherogenic lipids [34].

CONCLUSION:

Hyperthyroidism is associated with decrease levels of lipoprotein, caused by increased hepatic uptake due to an enhanced affinity for the LDL receptor, and regulatory protein of TG.

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