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STUDY OF THE ASSOCIATION BETWEEN SERUM LIPID PROFILE ABNORMALITIES AND HYPOTHYROIDISM

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ABSTRACT

Background/ Objective: *Hypothyroidism is a common endocrine problem in which the thyroid gland does not produce enough thyroid hormone. Hypothyroidism results from reduced secretion of total thyroxine (T4) and triiodothyronin (T3). Thyroid hormones have an essential role in mobilization, synthesis and metabolism of lipids. Therefore the current study was designed to examine the contributive role of hypothyroidism in development of dyslipidemia.*

Methods and Materials: *Thyroid and lipid profile parameters were analyzed in 175 subjects (125 patients with hypothyroidism compared with sex-matched 50 euthyroid controls) with a mean age 47.6 years (ranged 23-58 years). All patients were attending the endocrinology clinics at King Hussein Medical Center during the period from 15 September 2015 to 27 June 2016. Fully automated analyzers were used to measure thyroid and lipid profile parameters. Data were analyzed using a statistical software SPSS version 20.0. The observed differences in values were analyzed for statistical significance using Student's t-test and p-value <0.05 was considered significant.*

Results: *It was found that the patients with clinical hypothyroidism have a significant increase in the mean of cholesterol, triglyceride and low density lipoprotein (LDL) (p<0.05). Non significant decrease of high density lipoprotein was observed in hypothyroid patients.*

Conclusion: *the present study supports the proposal said that there is an association between hypothyroidism and serum lipid profile, characterized by an increase in concentrations of total cholesterol, triglyceride and LDL and by decrease of HDL concentrations. However, patients with hypothyroidism should be monitored for deterioration of thyroid function and dyslipidimia at regular interval.*

Keywords: Hypothyroidism, Dyslipidemia, Lipid Profile, Euthyroid.

Introduction

Thyroid hormones are important regulators of intermediary metabolic processes. They affect mobilization, synthesis and degradation of lipids; although degradation is influenced more than synthesis ,thyroid dysfunctions are amongst the most abundant endocrine disorder worldwide second only to diabetes mellitus [1]. Thyroid diseases are conditions that affect the produced amount of thyroid hormones. Excess production causing hyperthyroidism while diminished production leads to hypothyroidism [2].

Hypothyroidism is associated with goiter, ataxia, myxoedema, weight gain, fatigue and consequently hypothyroidism is associated with dyslipidemia which increase the risk of endothelial dysfunction, hypertension and cardiovascular diseases [4]. Hypothyroidism is one of the pathological conditions most frequently associated with disorders of lipid metabolism and finally dyslipidemia is one of the major risk factors of coronary disease [5].

Overt hypothyroidism is characterized by hypercholesterolemia and a marked increase in LDL because of a decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver [6]. However the controversy persists regarding the lipids level in subclinical hypothyroidism and its clinical significance. Moreover it is likely to be a risk factor for atherosclerosis and coronary diseases.

Endocrine diseases are increasing worldwide. It has been estimated that 0.2% of death in world results from endocrine disorders of which Iodine deficiency has been a major cause [7]. Thyroid disorders other than iodine deficiency disorders in the form of thyroiditis, hypothyroidism or autoimmune thyroid dysfunctions are on rise. The WHO estimates that substantially greater than 190 millions suffer from iodine deficiency disorders [7].

The prevalence of thyroid disorder is very high in our country also studies focusing on the association between thyroid function markers and dyslipidimia are sparse,

depends on these facts the current study was undertaken to investigate the alteration in the levels of serum lipid parameters in hypothyroidism Jordanian patients.

Methods and Materials

Subjects and samples

This study was carried out on 125 patients (23 male, 102female) (mean age 49.5). The control group includes 50 (13 male, 37 female) (mean age 45.7), all patients were attending the endocrinology clinic at King Hussein Medical Center during the period from 15 September 2015 to 27 June 2016; the members of both groups were enrolled in the study voluntarily. Detailed information of subjects was collected with the help of pre-test Performa that include age, sex and family or personal history of chronic disease. Ethical Committee approval was obtained for the collection of samples from the patients.

Venous blood samples were collected between 8:00 and 10:00 h into separated -jell tubes after a minimum 14 –h overnight fast. The samples were allowed to clot for 15 minutes at room temperature then similarly were centrifuged at 4000g for 10 minutes then analyzed immediately for lipid profile parameters.

Analysis

Study was carried out in Biochemistry Laboratory in Princess Iman Center for Research and Laboratory Sciences in King Hussein Medical Center in Amman-Jordan. The triglyceride, total cholesterol and high-density lipoprotein cholesterol concentrations (HDL-cholesterol) were measured using Cobas 501 auto-analyzer (Roche Diagnostics GmbH, Mannheim, Germany), levels of LDL-cholesterol were calculated by Friedwald formula. Serum TSH, free T4 and free T3 were measured using Cobas e 411 auto-analyzer (Roche Diagnostics GmbH, Mannheim, Germany), the corresponding Roche Diagnostics kits were used in analysis of all parameters

Reference range

Normal values for lipid profile parameters are total cholesterol (150-200 mg/dl), triglyceride (50-200 mg/dl), HDL-Cholesterol (10-60 mg/dl), LDL-Cholesterol (60-160 mg/dl), and total cholesterol/ HDL-Cholesterol is 4 mg/dl.

The normal references ranges for thyroid parameters according to kits were: TSH (0.4-4.2 μIU/ml), free T4 (0.5-1.9 ng/ml) and free T3 (0.4-4.0 μg/ml), so hypothyroidism was defined clinically by clinically TSH ≥ 4.5 μIU/ml.

Statistical analysis

Results are reported as mean ± standard deviation (SD), All statistical analysis were performed using SPSS for windows 20.0 (SPSS Inc. Headquarters, Chicago, III., USA) software program and Microsoft Excel 2007 program. Their observed differences in mean ± SD values were analyzed for statistical significance using Student's t-test and *P*-value < 0.05 was considered to be statistically significant

Results

The study included 125 patients (23 male, 102 female) (mean age 49.5 year). The control group includes 50 (13 male, 37 female) (mean age 45.7 year), all patients were attending the endocrinology clinic at King Hussein Medical Center during the period from 15 September 2015 to 27 June 2016.

The mean age of patients was 49.5 years and that of control was45.7 years *(p* = 0.0368). The 82 % patients and 74% of controls were female; 18% of patients were male in comparison with 26 % of healthy group. Therefore, overall the current study population shows a female predominance.

Table 1 summarize the lipid profile parameters of the study subjects in comparison with control group, the mean total serum cholesterol, triglyceride and LDL cholesterol levels were significantly higher in patient group (*p*< 0.05) . The mean serum HDL cholesterol levels were found significantly lower in patient group in comparison with that in healthy group.

Table 1: Lipid profile parameters of study subjects.

parameters	Control	Patient	*p-value*
	Mean ±SD	Mean ±SD	
TC	206.55 ± 8.99	243.77 ±13.6	0.034
TG	167.13 ± 9.32	189.98 ±12.7	0.024
HDL-C	41.45 ±5.66	47.88 ±7.43	0.02
LDL-C	118.24 ± 7.54	144.34 ± 4.88	0.04

Discussion

Thyroid function regulates a wide array of metabolic parameters, lipoproteins metabolism and some cardiovascular disease (CVD) risk factors are significantly affected by thyroid function [3, 4]. In high concentration of TSH, there are a linear increasing of total cholesterol, triglyceride, and LDL-C, and there are linear decreases in HDL-C, our findings are in consisting with other studies [8].

The thyroid hormones induce 3–hydrox–3–methylglutaryl -coenzyme A (HMG-CoA) reductase, which is the first step in cholesterol biosynthesis. Moreover, T3 up regulates LDL receptors by controlling the LDL receptor gene activation [8].

Furthermore, T3 controls the sterol regulatory

element-binding protein-2 (SREBP-2), which in turn regulates LDL receptor's gene expression [10]. T3 has also been associated with protecting LDL from oxidation [11]. This may explain the results of present.

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 [8]. 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) [12][13].

In the current study, the mean total serum cholesterol, triglyceride and LDL cholesterol levels were significantly higher in hypothyroid group, while the mean serum HDL cholesterol levels were found significantly lower in this group when compared with that in healthy group ,our findings are similar with what was found in previous studies. It was found that total plasma cholesterol and LDL cholesterol mean levels were higher in hypothyroidism patients than that in control subjects [14]. In another investigation, mean serum total cholesterol level was found elevated in primary and secondary hypothyroidism [15]. In previous studies it was found that triglyceride level elevated in hypothyroid cases [16-18]. So, our study findings parallel with the previous studies done by other investigators. It has been stated that decreased activity of LDL receptors as the main cause of hypercholesterolemia in hypothyroidism [19, 20].

Increase in HDL cholesterol concentration is mainly due to increased concentration of HDL2 particles [18]. It has been mentioned that decreased activity of CETP (cholesteryl ester transport protein) results in reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing HDL cholesterol levels [21]. Lam in pervious study stated that in hypothyroid patient's decreased activity of hepatic lipase leads to the decreased catabolism of HDL2 particles which leads to increased HDL [22]. Therefore, decrease in HDL cholesterol level in our study might be due to increased activity of CETP and lipoprotein lipase in hypothyroid patients.

Results of our study suggest that there is a strong association between dyslipidemia with hypothyroid patients. Therefore, patients presenting with dyslipidemia are recommended to be investigated for hypothyroidism. As our sample size was small and duration of study was limited, another study with large sample size and longer duration is also recommended.

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