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ORIGINAL RESEARCH

ALTERATIONS IN LIPIDS LEVEL IN SUBCLINICAL HYPOTHYROIDISM

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ABSTRACT:
Background: Although overt hypothyroidism is linked to lipid metabolic abnormalities, there are mixed results when it comes to the degree of lipid alterations in subclinical hypothyroidism (SCH).
Patients and Methods: In a cross-sectional investigation, the serum lipid parameters of 70 patients with subclinical hypothyroidism and 100 age and sex matched euthyroid controls were assessed.
Results: Patients with SCH had significantly higher mean serum total cholesterol (TC), triglycerides (TG), and very low-density cholesterol (VLDL) than controls (P<0.05). Patients with serum thyroid stimulating hormone (TSH) greater than 10 mU/L had higher mean TC, TG, and low-density cholesterol (LDL) concentrations than those with serum TSH equal to or less than 10 mU/L, although the difference was not statistically significant. The concentration of blood high-density cholesterol (HDL-C) and the amount of serum TSH had no correlation.
Conclusions: High TC, TG and VLDL were observed in our patients with SCH.
Keywords: Hypothyroidism; Lipids; LDL; VLDL; TSH

INTRODUCTION:

Thyroid stimulating hormone (TSH) concentrations in the blood are usually between 0.4 and 4.2 IU/mL. An increased blood TSH level with a normal serum free T4 (FT4) concentration is described as subclinical hypothyroidism (SCH)[1,2]. It is hypothesized to be linked to hypothyroidism with few or no clinical symptoms. Mild hypothyroidism, early thyroid failure, preclinical hypothyroidism, and low thyroid reserve were previously used

terminology for subclinical hypothyroidism. The prevalence has been estimated to be between 6 and 8% in women and 3% in men (up to 10 % in women more than 60 years)[3]. Hashimoto's disease is present in approximately 54% of individuals with subclinical hypothyroidism, as evidenced by increased serum concentrations of anti-thyroid microsomal or anti-thyroid peroxidase antibodies [4].

In some cases, subclinical hypothyroidism can proceed to overt hypothyroidism and be linked with clinical symptoms, requiring therapy [5]. Non-thyroidal disease, assay variability, pulsatile TSH secretion, nocturnal increase in TSH secretion, Heterophilic antibodies, TSH secreting pituitary adenomas, metoclopramide, and domperidone thyroid hormone resistance syndromes are some of the additional causes of elevated serum TSH.

Thyroid hormones play an important role in lipid and glucose metabolism. They control a variety of metabolic processes, including lipid metabolism. [6] Hypothyroidism is connected to a significant increase in blood levels of low-density lipoprotein (LDL), which can contribute to coronary artery disease[7]. In certain studies, increased TSH was found to cause a linear rise in total cholesterol, LDL, and triglyceride (TG) levels, as well as a linear decline in high-density lipoprotein cholesterol (HDL) levels, even within the normal range of TSH levels[8]. A rise in total cholesterol and LDL is linked to a variety of changes in synthesis, metabolism, and fat mobilization[9]. Thyroid hormones increase the activity of the liver enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-COA) reductase, which lowers cholesterol levels.

Thyroid hormones also boost cholesterol absorption from the colon by increasing LDL receptors on fibroblasts, liver, and other organs. These hormones also control cholesterol excretion from the gut via bile acids, as well as HDL cholesterol levels and hepatic lipase activity[9]. While some studies have discovered a relationship between subclinical hypothyroidism and an increased risk of atherosclerosis-related cardiovascular illness, others have not[9,10]. Although the effects of subclinical hypothyroidism on serum lipids are unknown, the changes seen in clinical hypothyroidism should be seen in subclinical hypothyroidism as well, albeit to a lower level. Various researches have looked into the relationship between lipid issues, SCH, and thyroid hormone levels in patients, with mixed results[11,12]. The goal of this study is to find out alterations in lipids level among patients with subclinical hypothyroidism.

MATERIAL AND METHODS:

This case control study was conducted in a tertiary care hospital among patients with subclinical hypothyroidism who were outpatients in the Department of General Medicine at National Capital Region Institute of Medical Sciences, Meerut. Seventy patients with SCH were compared to 100 healthy controls who were age, sex, and BMI matched. TSH levels larger than 6.5 mU/L, normal FT4 (0.89-1.76 ng/dL), and normal free T3 (2.30-4.20 pg/mL) levels were all required for inclusion. Healthy persons with normal thyroid functions who were the same age, gender, and BMI were recruited as controls.

Obese people with a BMI greater than 30 kg/m^2, current smokers and alcoholics, diabetes mellitus, renal insufficiency (serum creatinine> 1.5 mg/dL), hepatic failure, diagnosed hypothyroidism or those already on treatment, polyglandular disorders, thyroid cancer,

pregnant females along with females planning for pregnancy, positive anti TPO antibody test, patients having goiter and people with a history of antipsychotic treatment or oestrogen intake were all excluded.

All patients and controls were asked to provide a comprehensive medical history. Following informed consent, all patients and controls underwent a complete physical examination as well as the following tests: complete blood count (CBC), liver function test (LFT), kidney function test (KFT), fasting blood glucose, lipid profile including TC, TG, HDL-C, VLDL, and low density lipoprotein cholesterol (LDL-C), and thyroid function tests including serum TSH, free T4, and free T3. Hormonal assays were performed using commercial kits in duplicate and according to supplier protocols.

All continuous variables were presented as mean standard deviation. The chi-square test was also used to examine categorical variables. All of the findings were analyzed at a 5% level of significance, with a P value of <0.05 considered significant. The statistical analysis was performed using the Statistical Package for Social Sciences version 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS:

The mean age and BMI of SCH patients and healthy controls were similar (patients' mean age was 36.5 10.1 years, whereas controls' mean age was 34.5 10.3 years (P value = 0.208). Patients' BMI was 23.67 2.39 kg/m2, while controls' BMI was 23.06 2.53 kg/m2 (P = 0.066). Both patients with SCH and controls had a female preponderance. Subjects had considerably greater mean serum TC, TG, and VLDL than controls (Table 1). The average serum TC in the subjects was 182.91 41.01 mg/dL, compared to 170.19 34.36 mg/dL in the controls (P = 0.03). The mean serum TG in the subjects was 173.79 99 mg/dL, compared to 138.67 57.40 mg/dL in the controls (P = 0.00).Subjects had a mean serum VLDL of 34.83 19.75 mg/dL compared to 28.12 11.36 mg/dL in controls (P = 0.00). There was no statistically significant difference in LDL and HDL-Cholesterol levels between SCH patients and controls (Mean serum TC, TG, and LDL-C concentrations were higher in patients with serum TSH greater than 10 mU/L than those with serum TSH equal to or less than 10 mU/L, but this difference was not statistically significant) (Table 2). Patients with TSH higher than 10 mU/L had a mean serum TC of 192.50 35.04 mg/dL, compared to 173.86 44.55 mg/dL in patients with TSH equal to or less than 10 mU/L (P value = 0.055). Patients with TSH higher than 10 mU/L had a mean serum TG of 187.21 115.33 mg/dL, compared to 161.14 80.255 mg/dL in patients with TSH equal to or less than 10 mU/L (P value = 0.274). Mean serum LDL-C was 112.66 35.52 mg/dL in patients with TSH greater than 10 mU/L versus 98.64 39.61 mg/dL in subjects with TSH equal to or less than 10 mU/L (P value = 0.123). There was no correlation between blood HDL-C concentration and serum TSH level, however. Patients with serum TSH > 10 mU/L had somewhat higher VLDL levels than those with serum TSH 10 mU/L. (Table 2).

Table 1: Baseline Characteristics and Serum Lipid Profile in Patients with Subclinical Hypothyroidism and Healthy Controls

Parameter	Patients With SCH, n = 70	Healthy Controls, n = 100	P Value
Age, y	36.5±10.1	34.5±10.3	0.208
BMI, Kg/m2	23.67±2.39	23.06±2.53	0.066
Total Cholesterol, mg/dL	182.91±41.01	170.19±34.36	0.03
Triglyceride, mg/dL	173.79±99.00	138.67±57.40	0.00
LDL-Cholesterol, mg/dL	105.45±38.07	99.52±31.70	0.27
HDL-Cholesterol, mg/dL	42.27±7.77	41.89±7.52	0.75
VLDL, mg/dL	34.83±19.75	28.12±11.36	0.00

Table 2: Lipid Parameters Based on Serum TSH Level in Patients With Subclinical Hypothyroidism

Lipid Fraction, mg/dL	TSH (> 6.5 to ≤ 10), mU/L	TSH (> 10), mU/L	P Value
Total cholesterol	173.86 ± 44.55	192.50 ± 35.04	0.055
Triglyceride	161.14 ± 80.25	187.21 ± 115.33	0.274
LDL-cholesterol	98.64 ± 39.61	112.66 ± 35.52	0.123
HDL-cholesterol	42.03 ± 7.37	42.53 ± 8.328	0.790
VLDL-cholesterol	32.36 ± 15.97	37.45 ± 23.06	0.284

DISCUSSION

Increased TC and LDL-C levels are linked to overt hypothyroidism and an increased risk of cardiovascular disease. LDL clearance is hindered, resulting in an increase in plasma LDL-C, which is likely owing to decreased LDL receptor expression[13]. SCH and serum lipids have been the subject of numerous studies over the last 20 years, but the relationship between the two has remained a mystery. The literature on the relationship between SCH, serum lipids, and cardiovascular disease has produced mixed results[14,15]. After adjusting for age, race, sex, and use of lipid-lowering medicines, SCH was not linked with changes in TC, LDL-C, TG, or HDL-C among 8586 adults from the National Health and Nutrition Examination Survey III database[16]. There were no significant variations in blood TC, LDL-C, HDL-C, or TG between patients with SCH and the euthyroid control group, according to Vierhapper et al[17].

We discovered that SCH had no effect on mean HDL-C. Individuals with a serum TSH of more than 10 mU/L had a more aberrant lipid pattern[18,19]. Total TC, TG, and LDL-C concentrations were higher in patients with serum TSH greater than 10 mU/L than in

individuals with serum TSH equal to or less than 10 mU/L in the current study. Women with polycystic ovarian syndrome and SCH had considerably greater serum levels of TC and TG than women with polycystic ovary syndrome and normal thyroid functioning, according to a study from our institute[20]. Patients with autoimmune disorders had significant changes in their lipid profile[21]. Increases in TC, TG, and lipoproteins have been linked to thyroid autoimmunity in studies, however one study found no link between the two[22,23]. The presence of thyroid autoantibodies in our patients was not assessed. The abnormalities in lipid parameters discovered in this study could be linked to some genetic changes in the population.

Disparate study results might be caused by a variety of factors. Patients' ages, ethnicity, gender, and the severity and duration of hypothyroidism differed between studies. Furthermore, most observational studies did not account for changes in insulin resistance and smoking habit, which were identified as potential moderators of the thyroid-serum-lipids relationship. Smokers and individuals with insulin resistance have higher LDL-C levels in hypothyroid patients[24].

CONCLUSION:

Subclinical hypothyroidism is a serious disorder that has received little attention. It was linked to a considerable increase in blood Total Cholesterol and LDL-C levels, both of which are highly atherogenic, in the current investigation. In our SCH patients, we found high levels of TC, TG, and VLDL. When it comes to lipid profile pattern and SCH, the results are mixed. This could be related to the different populations studied, as well as age, gender, and ethnicity disparities. Because of the cross-sectional character of this study, assigning causality to any of the associations we discovered is problematic. To support a causal link, more longitudinal data would be needed to evaluate this association. As a result, it's critical to discover this illness early so that proper measures can be done to avoid potentially fatal complications.

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