



A Case Control Study of Serum Lipid Level Alterations in Subclinical Hypothyroid Patients

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Abstract

Background: *Subclinical hypothyroidism is often associated with increased risk of heart complications and various biochemical abnormalities.*

Objectives: *The present study was aimed to determine lipid abnormalities in the subclinical hypothyroidism patients.*

Methods: *The 1-year case-control study included 25 patients diagnosed with subclinical hypothyroidism and 25 euthyroid controls. Patients underwent thyroid and lipid profiling, evaluation of fasting blood sugar levels, complete blood count, and levels of apolipoprotein A and B. Statistical analysis was performed using chi-square test and unpaired t-test. $P < 0.05$ was considered as statistically significant.*

Results: *Female preponderance was observed with mean age of 20.46 ± 1.68 and 37.25 ± 13.73 years in euthyroid and subclinical hypothyroid group, respectively ($P < 0.001$). Mean body mass index of the euthyroid and subclinical hypothyroid groups was 21.58 ± 2.8 kg/m² and 20.46 ± 1.68 kg/m², respectively ($P = 0.033$). Thyroid-stimulating hormone (7.89 ± 2.51 vs. 2.07 ± 1.01 μ IU/ml; $P < 0.001$), serum cholesterol (168.08 ± 39.35 vs. 143.68 ± 38.15 mg/dL; $P = 0.031$) and triglyceride (162.02 ± 71.87 vs 121.48 ± 34.42 mg/dL; $P < 0.001$) levels were elevated in subclinical hypothyroid group when compared to euthyroid group. In the subclinical hypothyroid group, mean apolipoprotein A levels varied (117.04 ± 19.27 vs 96.48 ± 7.38 mg/dL; $P < 0.001$); however, apolipoprotein B levels were unaltered.*

Conclusion: *Alterations in lipid levels were observed in subclinical hypothyroidism patients which could be further established in future studies by the exploration of factors such as detection of autoimmune disorders in larger sample size.*

Keywords: *Serum cholesterol; Subclinical hypothyroidism; Triglycerides, Thyroid stimulating hormone.*

Introduction

Thyroid hormones such as thyroid-stimulating hormone (TSH) play an important role in lipid metabolism, and hence their deficiency often leads to development of dyslipidemia due to elevated levels of cholesterol, low-density lipoproteins (LDL), and triglycerides⁽¹⁾. Cardiovascular

diseases are among the complications caused due to hyperlipidemia, a form of dyslipidemia commonly observed in patients with hypothyroidism^(2,3).

Several studies have reported the variations in lipid levels, especially the levels of triglycerides, cholesterol, low-density and high-density lipoproteins but the alterations in thyroid-stimulating

hormone and apolipoproteins have not been extensively analyzed. Thus, the present study was conducted to investigate these abnormalities in patients with subclinical hypothyroidism (SCH).

Methodology

The present one-year case-control study was conducted between January 2011 and December 2011. The study included 25 patients in the SCH group and 25 euthyroid controls. Prior to the commencement of the study, an ethical clearance was obtained from the Ethical and Research Committee. Selected patients were informed about the purpose of the study before obtaining written consent.

Patients aged 18 years or more with elevated thyroid stimulating hormone level ($>5\mu\text{IU/mL}$), normal free triiodothyronine (T3) level (between 1.45 to 3.48 ng/mL), and normal free thyroxine (T4) level (0.7 to 1.85 ng/mL) were included in the SCH group for the evaluation of lipid levels. Patients with familial hypercholesteremia, end-stage renal disease, myocardial infarction, congestive cardiac failure, type 2 diabetes, overt hypothyroidism (especially on treatment with thyroxine and antithyroid drugs), and acute medical illness were excluded from the study. Women on oral contraceptives or pregnant were also excluded from the study.

Physical examination involved—pulse, blood pressure, thyroid swelling, tremors, skin changes, edema, pallor and lymph adenopathy, anthropometry (height, weight, and body mass index),^(4,5) and systemic examination. Demographic data including age and sex of the subjects were also recorded. The patients subsequently underwent examination of complete blood count, fasting blood sugar level, thyroid profile⁽⁶⁾, fasting lipid profile (total cholesterol, triglycerides, high-density and low-density lipoproteins),⁽⁷⁾ and apolipoproteins A and B⁽⁸⁾. Thyroid profiling and estimation of apolipoproteins were performed using a fully automated immunofluorescence immunoassay

analyser (Abott AxSYM) and 4010 Semiautoanalyser (Erba Trans Asia), respectively. Microsoft excel worksheet was used for coding of the data. The categorical data were analyzed using chi-square test and the continuous data were compared using unpaired t-test and was expressed as mean \pm standard deviation (SD). $P < 0.05$ was considered as statistically significant.

Results

Women predominance was observed in the SCH (96%) and euthyroid (64%) group, respectively. The prevalence of weight gain, neck swelling and fatigue was observed to be more in SCH patients (Figure 1). The mean values for age, BMI, levels of TSH, free T3, free T4, serum cholesterol, low density and high - density lipoprotein, triglycerides, Apolipoprotein A and B as observed from patients of euthyroid and SCH groups have been represented in Table 1.

Table 1. Mean values of study variables in euthyroid and SCH groups

Variable	Mean \pm SEM		P value
	Euthyroid	SCH	
Age	20.46 \pm 1.68	37.25 \pm 13.73	< 0.001
BMI	21.58 \pm 2.8	20.46 \pm 1.68	0.099
TSH	2.07 \pm 1.01	7.89 \pm 2.51	< 0.001
Free T3	2.04 \pm 0.52	2.04 \pm 0.39	1.000
Free T4	1.03 \pm 0.33	1.00 \pm 0.29	0.631
Serum cholesterol	143.68 \pm 38.15	168.08 \pm 39.35	0.031
Triglycerides	121.48 \pm 34.42	162.20 \pm 71.87	0.017
Low density lipoprotein	90.16 \pm 20.43	102.37 \pm 41.18	0.197
High density lipoprotein	38.00 \pm 5.86	42.08 \pm 9.80	0.087
Apolipoprotein A	96.48 \pm 7.38	117.04 \pm 19.27	< 0.001
Apolipoprotein B	99.12 \pm 9.22	94.58 \pm 15.2	0.175

Discussion

SCH has been recognized as an independent risk factor for myocardial infarction and aortic atherosclerosis. The present study supports the hypothesis that altered lipid levels are related to the SCH condition, which can further give rise to complications such as cardiovascular risk in SCH patients. The present study, by its findings, also adds to the existent literature on importance of analyzing lipid abnormalities in SCH patients among the Indian population.

Prevalence of hypothyroidism increases with age and is often observed to be higher in cases of

women than in men,⁽⁹⁾ which is in accordance with the present study. Majority of the patients were within 30 to 60 years of age in both the groups, which was comparable to other studies^(10, 11). However, Hennessey and Espailat⁽¹²⁾ suggested the need for modification of reference limit in geriatric population for diagnosing thyroid dysfunction. Thyroid hormone analysis in the present case-control study revealed significantly higher mean TSH level of the SCH group as compared to the euthyroid group, in contrast to the results of the comparison of free T3 and T4 levels, between the groups. In addition, the free T3 and T4 levels between the groups in the present study were similar, consistent and within the normal range, similar to the observation by Walter et al. (2012)⁽¹³⁾.

In the present study, the mean values of serum cholesterol, triglycerides and apolipoprotein A was significantly high in the SCH group. Elevation in the levels of HDL and LDL was also observed. In contrast, the level of apolipoprotein B was lower in the SCH groups as compared to the euthyroid group. Similar results were also observed by various studies. High serum cholesterol levels were also observed by Singh and Singh (2011)⁽¹⁴⁾. Khan *et al.*, Liu *et al.*, Saini *et al.*, and Rizos *et al.* have supported the present study by observing elevation in triglyceride levels among the SCH patients⁽¹⁵⁻¹⁸⁾. The elevation of apolipoprotein A and low level of lipoprotein B in the SCH patients were also observed in the study conducted by Peppas *et al.* (2011)⁽¹⁹⁾.

The presence of strong association between altered lipid levels and SCH have been suggested by several studies^(20,21). The altered levels of atherogenic lipids in SCH patients also indicates that SCH state may be responsible for altered lipid condition, as suggested by Jayasingh and Puthuran⁽²¹⁾. Higher level of triglyceride in SCH patients points toward a risk for the development of cardiovascular diseases such as atherosclerosis⁽²²⁾. In addition, elevated levels of LDL acts as an independent factor for the development of cardiovascular diseases and therefore several

therapy target the levels of LDL for reducing the risk of these complications⁽²³⁾.

In the recent times, the use of LDL as a diagnostic factor has faced certain limitations, leading to the analysis of other biochemical factors for improving the risk prediction in certain patients. Apolipoprotein B, one of the key components of all atherogenic lipoproteins, has been conjugated with LDL in this regard as the mean level of apolipoprotein B is an indicative of total number of atherogenic lipoproteins⁽²³⁾.

Even though the level of atherogenic lipoproteins has been elevated in SCH patients in the present study, contrastingly the mean level of apolipoprotein B has been observed to be low. According to Onat *et al.*, apolipoprotein B is an indicator of only the level of LDL in the serum. There is no correlation between the protein level and LDL-cholesterol (LDL-C), which could explain the contrasting results of the present study⁽²⁴⁾. Further, high levels of triglycerides often alter the correlation between apolipoprotein B level and LDL-C in patients with metabolic syndrome⁽²⁵⁾. The lipid alterations are also observed in systemic autoimmune diseases as reported by Marwaha et al⁽²⁶⁾.

The present study therefore demonstrates the significance of altered lipid levels in subjects diagnosed with SCH. Possible therapies such as thyroxine replacement therapy for managing the lipid levels in SCH patients has been suggested by similar studies⁽²⁷⁾. The hormonal therapy is reported to have an impact on the levels of serum cholesterol and LDL-C, with less or no influence on serum levels of triglycerides and HDL-cholesterol⁽²⁷⁾. Treatment of hypothyroidism with the help of drugs such as levothyroxine has been another suggested therapy to reduce the risk of heart diseases and regulate dyslipidemia, to some extent⁽²⁸⁾.

The limitations of the study design must be taken into consideration while interpreting the findings of the present study. It was unknown whether the lipid level alterations preceded the thyroid abnormalities, because of which it could not be

stated definitely that which one of the factor lead to the other. In addition, several other factors such as larger sample size, risks of autoimmune disorders, level of TPO antibodies and smokers must be included in the future studies to observe and establish the link between SCH and dyslipidemia.

Conclusion

The present study showed significantly higher levels of triglycerides, serum cholesterol, and low-density lipoprotein levels in patients with subclinical hypothyroidism. Prior to the initiation of medical treatment, the patients with laboratory report of hypercholesterolemia and hypertriglyceridemia should therefore be further examined for serum thyroid hormones measurements; in particular, the TSH level to administer proper medications to prevent further health complications.

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Conflict of Interest: None

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