Research Article

Lipid profile and hs-CRP levels in patients with subclinical hypothyroidism

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Abstract

Background: Several studies have demonstrated significantly lower high density lipoprotein (HDL) and higher triglycerides, and higher C-reactive protein (CRP) levels, in patients with subclinical hypothyroidism (SCH).

Objective: The aim of this study was to assess the levels of serum lipids and hs-CRP in patients with SCH and find out the correlation between levels of TSH with lipids and highly sensitive CRP (hs-CRP) in SCH.

Materials and Methods: This study comprised 150 patients and equal number of controls. Thyroid profile, lipid profile, and hs-CRP levels were performed on venous blood samples. Lipid profile was done using fully automated analyzer—912 Hitachi. Thyroid profile was done by chemiluminescence method and the level of hs-CRP was measured using latex agglutination method.

Results: TSH positively and significantly correlated with total cholesterol (TC), low density lipoprotein (LDL)-cholesterol, triglycerides, and very low density lipoprotein-cholesterol and inversely and insignificantly correlated with HDL-cholesterol. TSH and hs-CRP levels were positively and significantly correlated in subclinical hypothyroid patients as compared with controls.

Conclusion: In view of this study, SCH becomes an important entity due to possible link between it and cardiovascular risk factors especially lipid abnormalities. Also, significant association between TSH and hs-CRP is an important finding in this study.

KEY WORDS: Subclinical hypothyroidism, hs-CRP, lipid profile

Introduction

Physicians frequently encounter patients with very mild thyroid dysfunction. Unlike overt hypothyroidism, these patients have normal levels of T_3 and T_4 with only elevated serum thyrotropin levels. This pattern of laboratory values is called subclinical hypothyroidism (SCH).[1] Several studies have demonstrated significantly lower high density lipoprotein (HDL) and higher triglycerides, and higher CRP levels, in patients with SCH.[2] An association between hypothyroidism and hypercholesterolemia has been appreciated since the 1930s when animal studies demonstrated that hypothyroidism induced by high cholesterol feeding could be prevented by supplementation with thyroid preparation.[3] To find out the relationship between the serum cholesterol and SCH, many studies have been conducted. There are studies that shows higher levels of cholesterol is significantly associated with mild thyroid failure.[4–8] While in other studies, the differences were not seen to be statistically significant.[9–11] The role of hs-CRP in SCH as risk factor for coronary artery disease has given conflicting results with some studies showing positive correlation[12–14] while other studies fail to prove this association.

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So, this study was planned with the objective to assess the levels of serum lipids and hs-CRP in patients with SCH and to find out the correlation between levels of TSH with lipids and hs-CRP in SCH.

Materials and Methods

The present study was conducted on patients attending Medical Outpatient Department (OPD) of Government Medical College Hospital, Srinagar. The sample comprised 150 OPD patients diagnosed with SCH on abnormal thyroid function tests. Body mass index (BMI)-, age-, and sex-matched euthyroid controls in 1:1 ratio were also selected. The matching for age was done ±5 years. The controls were taken from those OPD patients whose thyroid function test (TFT) came normal. The patients who have fulfilled the following criteria were included in the study:

Inclusion Criteria

- 18-75 years old
- Persons of both sexes
- Persons having high TSH and normal T_3 and T_4
- Clinically euthyroid persons

Exclusion Criteria

- Persons with coronary artery disease
- Subjects on lipid lowering agents within 6 months before treatment
- Persons with diabetes or those with stroke
- Persons with a history of arthritis
- Smokers/alcohol users
- Persons using drugs that affect CRP levels—steroids, cyclosporine

Lipid profile was done using fully automated analyzer—912 Hitachi. Thyroid Profile was done by using chemiluminescence method and level of highly sensitive C-reactive proteins (hs-CRP) was measured using latex agglutination method.

Statistical Analysis

The data were analyzed with the help of computer software Microsoft Excel Version 10.0 for Windows. Primary outcome variables such as lipid profile, hs-CRP, TSH, and so on were reported as mean ± SD. Because of the non-normality of the variables concerned, non-parametric tests (Spearman's Rho) was used to evaluate correlation among the variables. Differences among patients with SCH and their corresponding controls were assessed by the unpaired t test. A *p* value of <0.05 was considered statistically significant.

Results

The mean age of patients in this study was 40.90 ± 13.77 years (mean ± SD) with a range of 18–75 years in cases while it was 42.63 ± 13.29 years (mean ± SD) in controls with a range of 18–72 years as shown in Table 1. Out of 150 patients and similar number of controls (1:1 ratio), 37 (25%) comprised males while 113 (75%) were females as shown in Table 2. Thus, male: female ratio was approximately 1:3.

Lipid Profile in Patients with SCH as Compared with Healthy Controls

Table 3 shows the value of total serum cholesterol in cases as 195.79 ± 29.86 mg/dL and 169.89 ± 19.90 mg/dl in controls. *p* Value (0.000) was found to be statistically highly significant. None of the subjects had total serum cholesterol more than 230.

Distribution of hs-CRP in Persons with SCH as Compared with Controls

The distribution of hs-CRP levels in patients with SCH as well as controls is shown in Table 5. Hundred (66.7%) persons with SCH had hs-CRP levels <1 mg/L, that is, low vascular risk. Five (3.3%) had hs-CRP levels between 1 and 1.99 mg/L, 13 (8.5%) had levels between 2 and 2.99 and 32 (21.5%) had hs-CRP levels >3 mg/L (high vascular risk). When compared with controls, 85 (56.7%) of controls had hs-CRP levels <1mg/L, 42 (28.3%) had hs-CRP levels l–1.99 mg/l, 8 (5.3%) had levels between 2 and 2.99, and 6 (10%) had hs-CRP levels >3 mg/l. The mean hs-CRP level was found to be 2.68–3.70 mg/L (mean ± SD) in controls. The *p* value was found to be statistically nonsignificant.

Discussion

Hypothyroidism is a disorder presenting with different degrees of thyroid failure and metabolic consequences. An increase of serum TSH is a very early biochemical marker of impending thyroid failure resulting from the gradual decline of T_4 and at a later stage of T_3. SCH is a frequent syndrome and has been defined as a condition with normal circulating levels of T_3 and T_4 but elevated TSH. Lipid levels and hs-CRP are known cardiovascular risk factors and the following study focuses on these two risk factors and their possible link with SCH.

Lipid Profile in Patients with SCH versus Controls

In this study, lipid profile was measured in both groups of subjects. Serum total cholesterol was found to be 197.5 ± 30.1 in SCH group versus 168.0 ± 20.8 in controls. The difference was highly significant (*p* = 0.000). The low density lipoprotein (LDL)-cholesterol values, when compared between two groups, were again found to be statistically significant (127.6 ± 30.9 in SCH versus 104.2 ± 17.8 in control group).

In the present study, the mean value of TSH was 14.20 ± 12.60, that is, >10 mU/L. So, the values obtained for TC and LDL were found to be significant. This was similar to other studies as done by Kung et al. (1995)[7], who found TC and LDL significantly higher than controls. The level of serum cholesterol was 232 mg/dl in cases versus 206 mg/dL in controls

Table 1: Age distribution in cases versus controls

Age groups	Cases			Controls		
(years)	Male	Female	Total	Male	Female	Total
18–29	0	23	23	3	15	18
30–41	20	55	75	15	58	73
42–53	5	15	20	7	20	27
54–65	7	15	22	5	17	22
66–77	5	5	10	7	3	10
Total	47	113	150	37	113	150

Table 2: Gender distribution of SCH patients

Sex	No. of patients	Percentage
Male	37	24.6
Female	113	75.4
Total	150	100

Table 3: Total serum cholesterol in SCH patients versus controls

Total cholesterol (mg/dL)	Cases		Controls	
	N	%	N	%
130–154	20	13.3	35	23.3
155–179	25	16.7	68	45.0
180–204	50	33.3	37	25.0
205–299	30	20.0	10	6.7
230–254	25	16.7	0	0
Total	150	100	150	100

Table 4: Correlation between TSH and lipid concentration in SCH patients

Lipid profile	TSH in SCH patients		
Total cholesterol	r = 0.56	$p < 0.01$	HS
Triglycerides	r = 0.48	$p < 0.01$	HS
LDL-cholesterol	r = 0.52	$p < 0.01$	HS
HDL-cholesterol	r = 0.09	$p < 0.273$	NS

R, Spearman Rho; HS, highly significant; NS, nonsignificant.

Table 5: Correlation between TSH and hs-CRP in SCH patients

	TSH in SCH patients		
hs-CRP	r = 0.453	$p < 0.01$	HS

R, Spearman's Rho; HS, highly significant.

(p <0 0005), while for LDL-cholesterol levels values were 152 in cases versus 135 in controls ($p < 0.005$). Another study by Hergenc et al. (2005)[15] showed that TSH positively and significantly correlated with TC (r = 0.211, $p = 0.001$ in men; r = 0.104, $p = 0.087$ in women) and for LDL-C (r = 0.208, $p = 0.002$ in men; r = 0.107, $p = 0.080$ in women).

hs-CRP in Patients with SCH versus Controls

In the present study, the mean hs-CRP was 2.59 ± 3.69 in SCH patients versus 1.97 ± 2.08 in controls. The levels, even though higher in patients with SCH, were statistically insignificant when compared with controls. Similarly, Lee et al. (2004)[16] also observed CRP value in patients with SCH and controls and found no significant difference. The findings of Luboshitzky and Herer (2004)[17] collaborated with the above study as the mean plasma CRP level in patients with SCH (3.7 ± 6.1 mg/L) were higher than that in controls (1.8 ± 1.3) but statistically not significant. So, was the findings in other studies as the one done by Hueston et al. (2005),[18] that is, NHANES survey.

This study showed hs-CRP levels <1 mg/L (low vascular risk) in 66.6% of patients with SCH compared to 56.6% in control group. About 3.33% of patients with SCH and 28.33% controls had hs-CRP levels in the range of 1–1.99 mg/L, while the levels were 2–2.99 mg/L in 8.33% SCH group versus 5% in controls. High vascular risk (level ≥ 3 mg/L) was found in 21.66% cases and in 11.6% controls. Luboshitzky and Herer (2004) found CRP levels ≥ 3 mg/L (high vascular risk) in 20.4% of patients with SCH versus 15.7% in controls.

Only few studies showed statistically significant values of hs-CRP than controls. One such study by Tuzcu et al. (2005)[14] found the mean value of hs-CRP in SCH patients in 4.2 ± 0.8 versus 1.05 ± -0.3 in controls ($p = 0.0001$).

Conclusion

In view of this study, SCH becomes an important entity due to possible link between SCH and cardiovascular risk factors, especially lipid abnormalities. Also, significant association between TSH and hs-CRP is an important finding in this study. In view of the findings of this study, SCH becomes an important entity to be screened for cardiovascular risk factors, and effect of replacement therapy on these risk factors need to be studied in order to reduce morbidity and mortality in these patients.

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