



Alteration of Lipid Profiles in Patients with Subclinical Hypothyroidism

Jung Eun Lee, Su Jin Jeong, Sol Jae Lee, Young Hoon Lee, Yuchang Lee, Sook Jung Lee, Chong Hwa Kim

Division of Endocrinology and Metabolism, Department of Internal Medicine, Sejong General Hospital, Bucheon, Korea

Objectives: Overt hypothyroidism has been associated with abnormalities of lipid metabolism; however conflicting results regarding the degree of lipid changes in subclinical hypothyroidism (SCH) have been reported. The aim of this study was to assess differences in lipid profile parameters between people with and without SCH in Korean population.

Methods: Serum lipid parameters of 37 patients with SCH and 44 euthyroid control subjects were evaluated in a retrospective cross-sectional study.

Results: The mean serum triglycerides (TG) level was significantly higher in patients with SCH than in controls ($p < 0.05$). The mean serum high-density lipoprotein cholesterol (HDL-C) level was significantly lower in patients with SCH than in controls ($p < 0.05$). When adjusted by age, the odds ratio for the association of HDL-C with SCH was significant at 0.893 (95% confidence interval 0.809-0.986) compared with that of the euthyroid controls. No association with SCH was found with total cholesterol level, low-density lipoprotein cholesterol level or serum thyroid-stimulating hormone level. In addition, the lipid profile did not differ significantly between premenopausal and postmenopausal women.

Conclusions: We found variations of lipid profiles in patients with SCH, characterized by a significantly lower HDL-C level. (J Lipid Atheroscler 2017 December;6(2):84-88)

Key Words: Subclinical hypothyroidism, Lipid

INTRODUCTION

It is well known that patients with overt hypothyroidism have elevated levels of cholesterol, low-density lipoprotein cholesterol (LDL-C), and apolipoprotein B.¹ Some studies have demonstrated dyslipidemia in patients with subclinical hypothyroidism (SCH).²⁻⁵

Hypercholesterolemia develops from a decrease in the fractional clearance of LDL-C due to a reduction in the number and activities of LDL receptors.⁶⁻⁸ SCH is defined

by high serum thyroid-stimulating hormone (TSH) concentration and normal serum total or free T4 and T3 concentrations, but with few or no symptoms and signs of hypothyroidism. SCH is more common among the elderly population, and is twice as common in women than in men.⁹ However there is a lack of studies on the association of SCH and dyslipidemia in Korea. Therefore, the objective of this study was to assess differences in lipid profile parameters between people with and without SCH in the Korean population.

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Corresponding Author: Chong Hwa Kim, Division of Endocrinology and Metabolism, Department of Internal Medicine, Sejong General Hospital, 28 Hohyeon-ro 489 Beon-gil, Sosa-gu, Bucheon 422-711, Korea
Tel: +82-32-340-1116, Fax: +82-32-340-1236, E-mail: drangelkr@hanmail.net

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Table 1. Baseline characteristics in subclinical hypothyroid patients and euthyroid controls

Parameters	Subclinical hypothyroid patients	Euthyroid controls	<i>p</i> value
Age (year)	58.08±13.06	47.05±9.52	<0.001
Sex			
Female (%)	51%	34%	-
Male (%)	49%	66%	
BMI (kg/m ²)	23.5±3.9	23.8±2.8	0.731
TSH (uIU/mL)	8.68±3.45	1.75±0.67	<0.001
Total T3 (pg/mL)	1.02±0.21	1.18±0.21	0.001
Free T4 (ng/dL)	1.15±0.20	1.34±0.14	<0.001
Total cholesterol (mg/dL)	182.3±45.8	186.4±29.9	0.625
Triglycerides (mg/dL)	158.6±98.7	107.9±69.3	0.008
HDL-C (mg/dL)	49.1±15.1	61.4±15.3	0.001
LDL-C (mg/dL)	113.6±37.8	114.8±28.8	0.869
Thyroglobulin Ab	34.2%		
Anti-microsomal Ab	36.8%		
Apolipoprotein A-I (mg/dL, n=21)	148.3±5.6		
Apolipoprotein B (mg/dL, n=21)	94.2±5.9		
Apolipoprotein A/B ratio	3.997±10.37		

Values are expressed as mean±standard deviation or number (%).

BMI; body mass index, TSH; thyroid-stimulating hormone, HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol, Ab; antibody.

p values were obtained by Student's *t*-test.

MATERIALS AND METHODS

1. Subjects

This cross-sectional study was conducted at Sejong General Hospital in Bucheon, South Korea. A total of 37 patients with SCH and 44 euthyroid controls were selected among individuals who visited the hospital from 2010 to 2017. The mean age of patients in SCH patients was 58.08 years old and euthyroid controls' mean age was 47.50 years old ($p<0.05$). Fifty one percent of SCH patients and 34% euthyroid controls were female, 49% percent of SCH patients and 66% euthyroid controls were male. The mean body mass index (BMI) in SCH patients was 23.5±3.9 kg/m² and BMI in euthyroid controls was 23.8±2.8 kg/m². SCH was established in terms of a TSH level >4.5 uIU/mL, with normal free T4 and total T3 levels. There was no history of thyroidectomy and cancer among the subjects. Patients taking any drug that could possibly affect lipid metabolism were excluded from the study. In total, 44 euthyroid controls (0<TSH levels ≤3.0 uIU/mL) were recruited among individuals visiting the health

promotion center for a health screening test. Premenopausal women were considered those under 50 years old and postmenopausal women were considered those over 50 years old.

2. Statistical analysis

All statistical computations were performed using the software program SPSS version 24.0 (SPSS Inc., Chicago, IL, USA). Data are reported as mean±standard deviation. The Student's *t*-test was performed to determine the significance of difference in the study parameters between the SCH group and controls. The Mann-Whitney test was also performed owing to the skewed distribution of certain parameters. Regression analysis was used to adjust for age. A *p* value less than 0.05 was considered to indicate statistically significant differences.

RESULTS

Table 1 shows the baseline characteristics in the SCH patients and euthyroid controls. The mean TSH level in

Table 2. The age-adjusted odds ratios (95% confidence interval) for lipid profiles in subclinical hypothyroid patients against euthyroid controls by regression analysis

Parameters	Euthyroid controls	Subclinical hypothyroid patients	<i>p</i> value
Total cholesterol (mg/dL)	1	1.080 (0.980-1.190)	0.121
Triglycerides (mg/dL)	1	0.997 (0.985-1.010)	0.683
HDL-C (mg/dL)	1	0.893 (0.809-0.986)	0.026
LDL-C (mg/dL)	1	0.925 (0.836-1.024)	0.132

HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol

p values were obtained by logistic regression analysis.

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Table 3. Distribution of lipid profile and thyroid hormone according to menopausal status

Parameters	Premenopausal women		
	Euthyroid controls (n=4)	Subclinical hypothyroid (n=15)	<i>p</i> value
TSH (μIU/mL)	1.05 (0.85-1.25)	7.80 (5.40-9.20)	0.001
Total T3 (pg/mL)	1.50 (1.25-1.60)	1.00 (0.90-1.20)	0.530
Free T4 (ng/dL)	1.00 (0.93-1.23)	1.00 (0.80-1.20)	0.270
Total cholesterol (mg/dL)	167.0 (109.8-209.3)	197.0 (181.0-214.0)	0.357
Triglycerides (mg/dL)	79.0 (49.3-144.8)	140.0 (109.0-193.0)	0.124
HDL-C (mg/dL)	69.0 (55.5-77.3)	52.0 (46.0-63.0)	0.808
LDL-C (mg/dL)	94.5 (40.3-130.8)	123.0 (99.0-133.0)	0.307

Parameters	Postmenopausal women		
	Euthyroid controls (n=11)	Subclinical hypothyroid (n=4)	<i>p</i> value
TSH (μIU/mL)	2.00 (1.60-2.60)	7.65 (6.56-13.28)	0.001
Free T4 (ng/dL)	1.30 (1.20-1.50)	1.20 (0.95-1.30)	0.280
Total T3 (pg/mL)	1.10 (1.10-1.40)	1.25 (0.90-1.45)	0.949
Total cholesterol (mg/dL)	186.0 (171.0-220.0)	210.5 (153.8-224.5)	0.753
Triglycerides (mg/dL)	73.0 (53.0-109.0)	124.0 (74.8-270.0)	0.078
HDL-C (mg/dL)	57.0 (51.0-84.0)	59.0 (40.5-81.3)	0.661
LDL-C (mg/dL)	113.0 (100.0-143.0)	133.5 (88.3-148.0)	0.851

Parameters	Premenopausal (n=19)	Postmenopausal (n=15)	<i>p</i> value
TSH (μIU/mL)	6.90 (5.10-8.70)	2.50 (1.80-6.30)	0.089
Free T4 (ng/dL)	1.10 (0.90-1.40)	1.30 (1.10-1.40)	0.302
Total T3 (pg/mL)	1.00 (0.90-1.20)	1.20 (1.10-1.40)	0.011
Total cholesterol (mg/dL)	195.0 (171.0-214.0)	199.0 (171.0-220.0)	0.758
Triglycerides (mg/dL)	132.0 (76.0-188.0)	87.0 (57.00-113.0)	0.071
HDL-C (mg/dL)	57.0 (50.0-67.0)	57.0 (49.0-84.0)	0.560
LDL-C (mg/dL)	118.0 (99.0-133.0)	117.0 (110.0-143.0)	0.656

Values are expressed as median (interquartile range)

TSH; thyroid-stimulating hormone, HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol

p values were obtained by Mann-whitney.

the SCH patients was 8.68 ± 3.45 μU/mL and that in euthyroid controls was 1.75 ± 0.67 μU/mL (normal value: 0.35-5.00) ($p < 0.001$). The mean total T3 level in the SCH

patients was 1.02 ± 0.21 pg/mL and that in euthyroid controls was 1.18 ± 0.21 pg/mL ($p = 0.001$). The mean free T4 level in the SCH patients was 1.15 ± 0.20 ng/dL and

that in euthyroid controls was 1.34 ± 0.14 ng/dL ($p < 0.001$). The mean total cholesterol level in the SCH patients was 182.3 ± 45.8 mg/dL and that in euthyroid controls was 186.4 ± 29.9 mg/dL ($p = 0.625$). The mean serum triglycerides (TG) value in the SCH patients was 158.6 ± 98.7 mg/dL and that in euthyroid controls was 107.9 ± 69.3 mg/dL ($p = 0.008$). The mean HDL-C value in the SCH patients was 49.1 ± 15.1 mg/dL and that in euthyroid controls was 61.4 ± 15.3 mg/dL ($p = 0.001$). The mean LDL-C value in the SCH patients was 113.6 ± 37.8 mg/dL and that in euthyroid controls was 114.8 ± 28.8 mg/dL ($p = 0.869$). Patients with SCH had a significantly higher level of TG and lower HDL-C level compared with euthyroid controls (Table 1). HDL-C showed a significant association with SCH based on the odds ratio and confidence interval (CI) 0.893 (95% CI=0.809-0.986), compared to that in euthyroid controls (Table 2). Among the total 34 females included in the study 19 (4 euthyroid controls and 15 SCH patients) were premenopausal and 15 (11 euthyroid controls and 4 SCH patients) were postmenopausal. There was no statistically significant difference in the lipid profiles between premenopausal and postmenopausal women (Table 3).

DISCUSSION

It is well known that thyroid hormones significantly affect lipoprotein metabolism. Thyroid hormones induce 3-hydroxy-3-methylglutarylcoenzyme A (HMG-CoA) reductase, which is the first step in cholesterol biosynthesis. T3 stimulates the upregulated expression of LDL receptor proteins and controls the sterol regulatory element binding protein-2 (SREBP-2), which in turn regulates the gene expression of LDL receptors and protects LDL-C from oxidative pathways. Thyroid hormones influence HDL-C metabolism by increasing cholesteryl ester transfer protein (CETP) activity.¹⁰ Many previous studies have shown that the serum total

cholesterol, TG and LDL-C levels were significantly increased, while the HDL-C level was decreased in hypothyroidism. A recent meta-analysis to investigate the association between SCH and lipid profiles suggested that the serum total cholesterol, LDL-C, and total TG levels were significantly increased in patients with SCH compared with those in euthyroid control subjects.¹¹ Many previous studies have suggested that patients with SCH had higher levels of total cholesterol and LDL-C compared with euthyroid controls. This trend is reasonable, given that LDL contains 65% total cholesterol. However, there has been some controversy regarding whether SCH induces dyslipidemia.

One of the main reasons contributing to these conflicting results among previous studies is that these analyses did not adjust for potentially confounding factors, such as age, sex, BMI, and alcohol consumption. Our study showed that HDL-C level in SCH patients was significantly lower. The lipid level differences between premenopausal and postmenopausal women were found to be statically insignificant. This finding was concordance with result of previous study.² This study has several limitations. First, the sample size was relatively small given the retrospective case-control study design; therefore a larger study would be required to improve the statistical power of the analysis. Therefore confounding variables, including age, sex, BMI, and alcohol consumption, need to be carefully adjusted and controlled in the study design; as a cross-sectional study, this was not possible in the present work. Further studies are needed to better understand the mechanism of dyslipidemia in SCH, including multicenter prospective larger studies with adjustment of confounding factors.

CONCLUSION

We found alteration of lipid profiles in patients with SCH, characterized by a significantly low HDL-C level.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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