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ORIGINAL ARTICLE

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Evaluation of the relationship of subclinical hypothyroidism with metabolic syndrome and its components in adolescents: a population-based study

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Abstract

Purpose This study investigated the association of subclinical hypothyroidism (SCH) with metabolic syndrome (MetS) and its components in adolescents.

Methods The study population included 1006 adolescents (aged 10–18 years) from the Korea National Health and Nutrition Examination Surveys; SCH subjects were compared with euthyroid subjects. MetS was defined using the International Diabetes Federation criteria. The risks of MetS and its components in SCH and euthyroid subjects were calculated using binary logistic regression analyses.

Results Study subjects had a mean age of 14.2 ± 2.5 years, and 53% were male. The prevalence of MetS was 2.5% in the overall study population (3.2% of males and 1.7% of females). Among the 1006 subjects, 143 (14.2%) had SCH. The risk of MetS was not higher in SCH subjects than in euthyroid subjects (odds ratio [OR], 1.50; 95% confidence interval [CI], 0.54–4.11); however, among the components of MetS, the risk of abdominal obesity was higher in SCH subjects than in euthyroid subjects (OR, 2.08; 95% CI, 1.04–4.15) after adjusting for age, sex, and body mass index (BMI). Although not statistically significant, a trend toward increased risk of elevated blood pressure (BP) was observed in SCH subjects relative to euthyroid subjects after further adjusting for age, sex, and BMI (OR, 2.01; 95% CI, 0.89–4.52). Furthermore, non-obese SCH subjects had higher systolic BP compared with non-obese euthyroid subjects after adjusting for age, sex, and BMI ($P = 0.014$).

Conclusions SCH was not associated with the presence of MetS. However, SCH may be associated with abdominal obesity and possibly elevated BP in adolescents.

Keywords Cardiovascular disease · Metabolic syndrome · Abdominal obesity · Elevated blood pressure · Subclinical hypothyroidism · Adolescents

Introduction

Subclinical hypothyroidism (SCH) is characterized by elevated serum thyroid-stimulating hormone (TSH) levels, with normal levels of free thyroxine (FT4) and free triiodothyronine. SCH can be classified into two categories according to the degree of serum TSH level elevation: mild (TSH 4.5–10 mIU/L) or severe (TSH >10 mIU/L) [1]. SCH in adults is associated with an increased risk for dyslipidemia, insulin resistance, coronary heart disease, and heart failure [2–5]. The current SCH treatment guidelines recommend levothyroxine for adults with serum TSH >10 mIU/L or with TSH <10 mIU/L in the presence of hypothyroidism symptoms, positive thyroid antibodies or evidence of atherosclerotic cardiovascular disease (CVD)

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[6]. In contrast, the association between SCH and adverse cardiovascular outcomes among children and adolescents is unclear, and the management of SCH remains a matter of debate, particularly in those with a mild form of SCH [7]. Several studies have examined the association between SCH and atherosclerotic risk factors, such as dyslipidemia or insulin resistance, with conflicting results among children [8–11].

Metabolic syndrome (MetS) is a cluster of disorders, including abdominal obesity, glucose intolerance, hypertension, and dyslipidemia. MetS is clearly associated with an increased risk for type 2 diabetes and CVD [12–14]. The prevalence of MetS in children, adolescents, and adults has increased worldwide in recent years [12, 15]. Because risk factors for the development of CVD begin in childhood and may be predictive of CV risk in adults, it is valuable to assess whether the risk of MetS is increased in pediatric SCH subjects compared with euthyroid subjects.

This study investigated the association between SCH and the presence of MetS in adolescents aged 10–18 years. We further determined which components of MetS were significantly associated with SCH.

Materials and methods

Study subjects

The data for this study were obtained from 2013 to 2015 Korea National Health and Nutrition Examination Survey (KNHANES), a nationally representative cross-sectional survey conducted annually by the Korea Centers for Disease Control and Prevention (KCDC). The KNHANES, comprising three sections (examination, health interview, and nutritional survey), targets the entire national population. From the 22,000 participants included in the KNHANES, we selected 2425 subjects aged 10–18 years. We excluded subjects with overt hypothyroidism or hyperthyroidism and those with missing data regarding free T4 or TSH levels. Furthermore, we excluded subjects with abnormal liver function (serum alanine aminotransferase [ALT] or aspartate aminotransferase [AST] levels ≥3-fold relative to the upper normal limit) or abnormal renal function (serum creatinine levels of 1.5 mg/dL for males or 1.4 mg/dL for females). Only two subjects with abnormal liver function were excluded, and all subjects had normal renal function (serum creatinine <1.2 mg/dL). Finally, a total of 1006 subjects (529 males and 477 females) were included in this study (Fig. 1). All participants signed written informed consent, and the institutional review boards of the Korea National Health Insurance Service and Catholic Kwandong University College of Medicine, International St. Mary's Hospital, approved the study protocol. This study was conducted according to the 1964 Helsinki Declaration-based ethical principles for medical research involving human subjects.

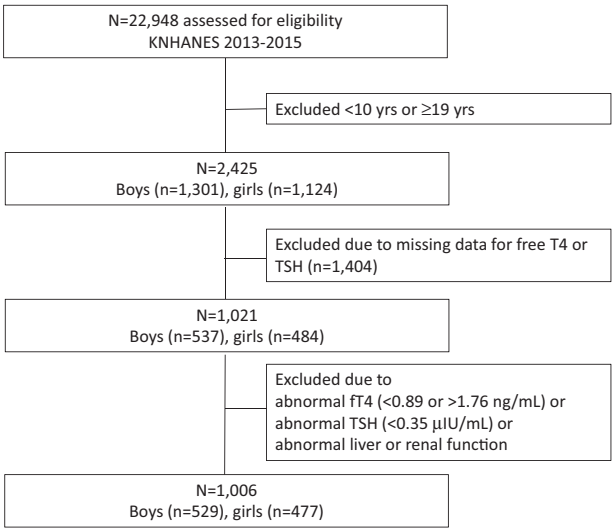

Fig. 1 Flow diagram of selection and exclusion of study subjects. TSH thyroid-stimulating hormone

Biochemistry assessment

Body weight and height were measured with subjects wearing light clothing and no shoes. An expert inspector measured weight to the nearest 0.1 kg using a scale (GL-6000–20, Seoul, Korea) and height to the nearest 0.1 cm using an extensometer (Seca 225; Seca GmbH, Hamburg, Germany). Body mass index (BMI) was calculated by dividing the weight (kg) by the height (m) squared. Obesity was defined as a BMI at or above the 95th percentile for adolescents of the same age and sex. Overweight was defined as a BMI at or above the 85th percentile and below the 95th percentile for adolescents of the same age and sex.

Waist circumference was measured to the nearest 0.1 cm at the midpoint between the lowest ribs and the iliac crest during exhalation. Blood pressure (BP) was measured three times using a mercury sphygmomanometer (Baumanometer® Desk Model 0320; WA Baum, Co., Copiague, NY, USA) after an appropriate tourniquet was applied to the right arm in subjects rested in a seated position for 5 min; the average of the second and third measurements was ultimately recorded as the BP.

As part of the KNHANES survey, blood samples were collected after an 8-h fast and then immediately processed, refrigerated, and transported in cold storage to a central laboratory (Neodin Medical Institute, Seoul, South Korea). All blood samples were analyzed within 24 h of collection. Fasting plasma glucose (FPG), the total

cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured using a Hitachi Automatic Analyzer 7600 (Hitachi Ltd., Tokyo, Japan). Glycated hemoglobin (HbA1c) was measured with an HLC-723G7 (Tosoh, Tokyo, Japan). Serum FT4 and TSH levels were measured with an electrochemiluminescence immunoassay using a commercial kit (Roche Diagnostics, Mannheim, Germany). Serum AST, ALT, and creatinine levels were measured using a Hitachi Automatic Analyzer (Hitachi, Tokyo, Japan) (reference range, < 40 IU/L for AST and ALT; 0.5–1.4 mg/dL for creatinine).

Definition of MetS and SCH

In this study, MetS was defined based on the International Diabetes Federation (IDF) criteria [16]. The diagnostic criteria for abdominal obesity incorporated waist circumference, as suggested by the 2007 Korean National Growth Chart for children and adolescents. For subjects aged 10–16 years, the following MetS criteria were used: abdominal obesity (≥90th percentile as assessed by waist circumference) and at least two of the following components: TG ≥ 150 mg/dL, HDL-C <40 mg/dL, systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg, and FPG ≥ 100 mg/dL or known type 2 diabetes mellitus. For subjects ≥ 16 years of age, the following MetS criteria were used: waist circumference ≥ 90 cm for males or ≥ 80 cm for females) and at least two of the following components: TG ≥ 150 mg/dL, HDL-C <40 mg/dL (males) or < 50 mg/dL (females), SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, and FPG ≥ 100 mg/dL or known type 2 diabetes mellitus. SCH was defined as a serum TSH level >4.5 μIU/mL with normal level of free T4 (reference range, 0.89–1.76 ng/dL) [17].

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA). Data are expressed as mean ± standard deviation for continuous variables or percentage for categorical variables. The characteristics of participants were compared using independent-sample *t* test for continuous variables and chi-squared test for categorical variables. We used analysis of covariance adjusted by age, sex, and BMI to compare metabolic parameters between non-obese euthyroid and non-obese SCH subjects. We performed multiple logistic regression analyses to calculate the odds ratios (ORs) of MetS and MetS components. A *P*-value < 0.05 was considered statistically significant, and confidence intervals (CIs) were calculated at the 95% level.

Results

Clinical and biochemical characteristics of study subjects

Table 1 lists the characteristics of study subjects according to sex. Subjects had a mean age of 14.2 ± 2.5 years, and 53% were male. BMI and systolic BP were higher in males than in females. TC and HDL-C levels were lower in males than in females; serum TG levels were similar in both sexes. FPG, AST, ALT, and serum creatinine levels were higher in males than in females. FT4 level was higher in males than in females, while TSH levels were similar in both sexes. Of the 1006 subjects, 143 (14.2%) were in the SCH group, and 863 had normal thyroid function. TSH levels in the SCH group ranged from 4.5 to 11.8 μIU/mL. Of the 143 SCH subjects, 139 (97.2%) had the mild form. Systolic BP and TC levels were higher in the SCH group than in the euthyroid group. There were no significant differences in waist circumference and BMI between groups; however, the prevalence of obesity (≥ 95th percentile of BMI of same age and sex) was

Table 1 Clinical and biochemical characteristics of study subjects

	Males ($n = 529$)	Females ($n = 477$)	*p*-value
Age (years)	14.2 ± 2.5	14.2 ± 2.5	0.660
Height (cm)	165.3 ± 11.3	157.6 ± 7.9	<0.001
Weight (kg)	59.6 ± 15.5	52.2 ± 11.1	<0.001
Waist circumference (cm)	73.2 ± 10.7	68.4 ± 8.2	<0.001
BMI (kg/m^2)	21.5 ± 3.9	20.9 ± 3.4	0.004
SBP (mmHg)	111.2 ± 10.1	106.2 ± 8.5	<0.001
DBP (mmHg)	66.2 ± 8.9	66.0 ± 7.9	0.738
Fasting glucose (mg/dL)	92.9 ± 7.4	90.2 ± 8.3	<0.001
HbA1C (%)	5.47 ± 0.29	5.44 ± 0.35	0.139
Total cholesterol (mg/dL)	154.7 ± 25.5	164.1 ± 25.3	<0.001
Triglyceride (mg/dL)	84.7 ± 53.2	84.5 ± 42.1	0.922
HDL cholesterol (mg/dL)	50.5 ± 9.7	52.8 ± 9.4	<0.001
AST (IU/L)	20.3 ± 6.9	17.2 ± 4.3	<0.001
ALT (IU/L)	17.1 ± 14.4	12.3 ± 7.2	<0.001
Serum creatinine (mg/dL)	0.78 ± 0.16	0.64 ± 0.10	<0.001
Free T4 (ng/dL)	1.32 ± 0.16	1.23 ± 0.15	<0.001
TSH (μIU/mL)	2.90 ± 1.57	2.80 ± 1.58	0.347

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HbA1C* glycated hemoglobin, *HDL* high-density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *T4* thyroxine, *TSH* thyroid-stimulating hormone

Data are expressed as the mean ± SD. $^*P < 0.05$, *P*-value between males and females

higher in the SCH group than in the euthyroid group (15.4 vs. 8.0%, $P = 0.004$). A higher trend in fasting glucose and TG levels was observed in the SCH group than in the euthyroid group, but no significant differences were detected.

We further classified the subjects into four groups according to their thyroid function and the presence of obesity (Table 2). Obese SCH subjects had higher systolic BP, higher TC levels, and lower HDL-C levels compared with non-obese SCH subjects, after adjusting for age and sex. There was a trend for higher TG levels in obese SCH subjects than in non-obese SCH subjects. Among the euthyroid groups, obese subjects had higher systolic BP, higher levels of TC and TG, and lower HDL-C than non-obese subjects (Table 2). However, there were no differences in BP, serum TC, TG, or HDL-C between the obese euthyroid and obese SCH groups (Table 2).

Prevalence and risk of MetS and its components according to thyroid function

The prevalence of MetS was 2.5% in the overall study population (3.2% of males and 1.7% of females). There were no differences in the prevalence of abdominal obesity or hypertriglyceridemia by sex (Table 3). Elevated BP and hyperglycemia were more prevalent in males than in females ($P < 0.001$ for both; Table 3). We examined the prevalence of MetS and its components according to the state of thyroid function (Fig. 2). The prevalence of MetS tended to be higher in the SCH group than in the euthyroid group, although the difference was not significant (4.2 vs. 2.2%, $P = 0.151$). However, abdominal obesity (17.6 vs. 9.6%, $P = 0.004$) and elevated BP (6.3 vs. 3.0%, $P = 0.048$) differed significantly in the SCH and euthyroid groups (Fig. 2).

The risk of MetS tended to be higher in adolescents with SCH than in euthyroid subjects, but this increase was not statistically significant (OR, 1.50; 95% CI, 0.54–4.11) in multiple logistic regression analyses (Table 4). With regard to MetS components, the ORs for abdominal obesity and elevated BP were significantly higher in adolescents with SCH than in euthyroid subjects after adjusting for age and sex (OR, 2.09; 95% CI, 1.28–3.42 and OR, 2.33; 95% CI, 1.04–5.17, respectively). After further adjusting for age, sex, and BMI, the risk of abdominal obesity remained significantly higher in SCH subjects than in euthyroid subjects (OR, 2.08; 95% CI, 1.04–4.15), although the risk of elevated BP was not statistically significant (OR, 2.01; 95% CI, 0.89–4.52). The risk of hypertriglyceridemia, low HDL-C, and hyperglycemia were not significantly different between groups (Table 4). Next, we analyzed the association between serum TSH level and components of MetS as continuous variables. Serum TSH level was positively associated with systolic BP ($\beta = 0.094$, $P = 0.034$) and serum TG ($\beta = 0.075$, $P = 0.017$) after adjusting for age, sex, and BMI.

Finally, we analyzed differences in metabolic parameters between non-obese euthyroid and non-obese SCH subjects

Table 2 Clinical and biochemical characteristics of study subjects according to thyroid function and obesity status

	Euthyroid group ($n = 863$)		SCH group ($n = 143$)	
	Non-obese ($n = 794$)	Obese ($n = 69$)	Non-obese ($n = 121$)	Obese ($n = 22$)
Age (years)	14.2 ± 2.5	14.5 ± 2.6	13.6 ± 2.6	15.2 ± 2.3
Sex (male, %)	416 (52.4%)	33 (47.8%)	67 (55.4%)	13 (59.1%)
BMI (kg/m^2)	20.5 ± 2.8	29.0 ± 3.2[a]	20.3 ± 2.7	29.1 ± 2.8[c]
Obesity (≥ 95th percentile of BMI)	0 (0.0%)	69 (8.0%)	0 (0.0%)	22 (15.4%)
SBP (mmHg)	107.8 ± 9.2	115.2 ± 11.0[a]	109.8 ± 9.8	118.1 ± 11.4[d]
DBP (mmHg)	65.9 ± 8.4	67.7 ± 8.3	66.1 ± 8.9	68.1 ± 8.9
Fasting glucose (mg/dL)	91.3 ± 7.1	93.0 ± 8.2[b]	92.3 ± 7.1	95.8 ± 23.4
HbA1C (%)	5.4 ± 0.2	5.5 ± 0.3	5.5 ± 0.2	5.6 ± 1.0
Total cholesterol (mg/dL)	157.6 ± 26.1	166.9 ± 24.6[a]	162.3 ± 23.5	171.9 ± 24.1[d]
Triglyceride (mg/dL)	80.9 ± 43.7	110.8 ± 59.6[a]	89.0 ± 60.2	110.6 ± 57.2
HDL cholesterol (mg/dL)	52.1 ± 9.3	44.6 ± 10.3[a]	53.3 ± 9.8	46.2 ± 7.5[c]
AST (IU/L)	18.5 ± 5.7	21.0 ± 7.7[a]	19.4 ± 6.5	19.2 ± 8.6
ALT (IU/L)	13.7 ± 9.9	26.6 ± 19.4[a]	14.0 ± 12.7	21.8 ± 14.4[d]
Serum creatinine (mg/dL)	0.72 ± 0.15	0.73 ± 0.16	0.68 ± 0.15	0.74 ± 0.16
Free T4 (ng/dL)	1.29 ± 0.16	1.27 ± 0.16	1.24 ± 0.15	1.22 ± 0.13
TSH (μIU/mL)	2.36 ± 0.95	2.37 ± 1.00	5.88 ± 1.27	5.65 ± 1.31

[a]$P < 0.01$, [b]$P < 0.05$ compared with non-obese euthyroid after adjusting for age and sex

[c]$P < 0.01$, [d]$P < 0.05$ compared with non-obese SCH after adjusting for age and sex

Table 3 Prevalence of metabolic syndrome and its components in the overall population by sex and thyroid function

	All (n = 1006)	Males (n = 529)	Females (n = 477)	P-value	Euthyroid (n = 863)	SCH (n = 143)	P-value
Metabolic syndrome (%)	2.5%	3.2%	1.7%	0.155	19 (2.2%)	6 (4.2%)	0.151
Components (%)							
Abdominal obesity	10.7%	11.0%	10.5%	0.839	83 (9.6%)	25 (17.6%)	0.004
Hypertriglyceridemia	7.9%	8.5%	7.1%	0.482	62 (7.2%)	17 (11.9%)	0.053
Low HDL cholesterol	15.3%	12.2%	18.7%	0.005	136 (15.8%)	19 (13.2%)	0.406
Elevated blood pressure	3.5%	5.5%	1.3%	<0.001	26 (3.0%)	9 (6.3%)	0.048
Hyperglycemia	11.0%	14.6%	7.1%	<0.001	93 (10.8%)	18 (12.6%)	0.522

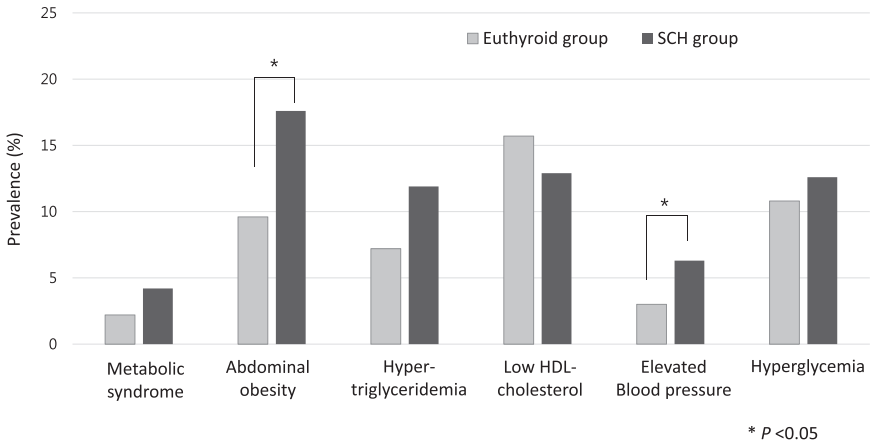

Fig. 2 Prevalence of metabolic syndrome and its components according to thyroid function state in the overall population. *$P < 0.05$ between groups

Table 4 Odds ratios for metabolic syndrome and its components in SCH subjects compared with euthyroid subjects after adjusting for age, sex, and BMI

	Non-adjusted		Age-, sex-adjusted		Age-, sex-, and BMI-adjusted	
	ORs (95% CI)	P-value	ORs (95% CI)	P-value	ORs (95% CI)	P-value
Metabolic syndrome	1.96 (0.76–4.99)	0.159	2.02 (0.79–5.18)	0.142	1.50 (0.54–4.11)	0.437
Components						
Abdominal obesity	2.01 (1.23–3.27)	0.005	2.09 (1.28–3.42)	0.003*	2.08 (1.04–4.15)	0.036*
Hypertriglyceridemia	1.74 (0.98–3.07)	0.055	1.73 (0.97–3.05)	0.060	1.57 (0.87–2.81)	0.127
Low HDL cholesterol	0.80 (0.47–1.35)	0.407	0.86 (0.50–1.48)	0.593	0.78 (0.44–1.36)	0.387
Elevated blood pressure	2.15 (0.98–4.69)	0.054	2.33 (1.04–5.17)	0.038*	2.01 (0.89–4.52)	0.091
Hyperglycemia	1.19 (0.69–2.04)	0.522	1.09 (0.62–1.88)	0.761	1.07 (0.61–1.84)	0.821

$P < 0.05$ in logistic regression analyses

Table 5 Age, sex, and BMI-adjusted mean values of metabolic parameters between non-obese euthyroid and non-obese SCH subject

	Non-obese euthyroid	Non-obese SCH	P-value
Systolic BP (mmHg)	107.8 ± 0.3	110.0 ± 0.7	0.014
Diastolic BP (mmHg)	65.9 ± 0.2	66.7 ± 0.7	0.26
Triglyceridemia (mg/dL)	80.9 ± 1.6	89.3 ± 4.1	0.064
HDL cholesterol (mg/dL)	52.1 ± 0.3	53.2 ± 0.8	0.223
Total cholesterol (mg/dL)	157.6 ± 0.8	162.1 ± 2.2	0.072
Glucose (mg/dL)	91.3 ± 0.2	91.8 ± 0.6	0.495

Data are expressed as mean ± SD

to elucidate the metabolic effects of SCH unrelated to obesity (Table 5). Non-obese SCH subjects had higher systolic BP compared with non-obese euthyroid subjects after adjusting for age, sex, and BMI ($P = 0.014$). Serum TC and TG levels were non-significantly higher in non-obese SCH subjects than in non-obese euthyroid subjects (Table 5).

Discussion

This study found no increase in the prevalence of MetS in adolescents with SCH, but SCH subjects had a higher risk of abdominal obesity compared with euthyroid subjects.

Various studies have investigated the associations between SCH and MetS in adults with inconsistent results [18–20]. One recent meta-analysis found that SCH was significantly associated with a higher risk of MetS in adults (OR, 1.31; 95% CI, 1.08–1.60; $P = 0.006$). It also found that a positive association was identified in studies using IDF criteria of MetS, but not in those using the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria [18]. Another meta-analysis reported no increase in the prevalence of MetS as defined by the NCEP-ATP III criteria in SCH subjects [19]. Waring et al. [20] conducted a prospective study involving older adults in the U.S. and found that SCH in subjects with a TSH > 10 mIU/L was significantly associated with an increased risk for prevalent MetS (OR, 2.3; 95% CI, 1.0–5.0; $P = 0.04$), but not with an increased risk for incident MetS (OR, 2.2; 95% CI, 0.6–7.5) during a six-year follow-up. To date, few studies have investigated the relationship of SCH with the components of MetS [8, 10, 11, 21, 22], and only one study examined the correlation between SCH and the composite state of MetS in children and adolescents [11]. This study found that TSH levels were higher in the MetS group than in the non-MetS group, although there was no increased prevalence of MetS in children with SCH than in euthyroid subjects [11].

Thyroid hormones affect the regulation of lipid synthesis and metabolism. Many studies have found elevated levels of serum TC, LDL-C, apolipoprotein B, and TG in subjects with overt hypothyroidism; however, the effects of SCH on serum lipid values are less clear [23]. In particular, several studies have investigated the association of SCH and lipid values in children and adolescents, with inconsistent results [8, 9, 11, 24]. Witte et al. [8] reported a positive association between TSH levels and TC, LDL-C, and TG in a large cohort of children and adolescents. In a study conducted in China, Zhang et al. reported a positive correlation between LDL-C, TG, and TSH levels [11]. Marwaha et al. [9] found no difference in serum TG and cholesterol between the euthyroid and SCH groups of children and adolescents, regardless of SCH severity. In this study, we observed a positive association between serum TG and TSH levels after adjusting for confounding factors. However, logistic regression analysis revealed no increased risk of hypertriglyceridemia in SCH, relative to the euthyroid group. The differing results among studies might be influenced by the relatively small study populations, severity of SCH, etiology or duration of SCH, and cross-sectional design. With regard to HDL-C, recently published studies [8, 11] found no significant association between HDL-C and TSH levels, although one small-scale study found decreased HDL-C levels in children with SCH [24]. Marwaha et al. [9] found decreased HDL-C levels in children with severe SCH (TSH > 10 mIU/L), but not in those with mild SCH (TSH < 10 mIU/L) compared with euthyroid healthy controls. We found no correlation between SCH and HDL-C levels and a similar prevalence of low HDL-C between SCH and euthyroid subjects. Most of our subjects had a mild form (TSH < 10 mIU/L) of SCH (97.2%), and our results are comparable with the findings of Marwaha et al. [9]. Interestingly, we found that after adjusting for age and sex, obese SCH subjects showed lower HDL-C, higher TC, and non-significantly higher TG levels compared with non-obese SCH subjects, but not when compared with obese euthyroid subjects. Moreover, among non-obese subjects, there was no significant difference in lipid profiles between euthyroid and SCH subjects. These findings suggest that obesity more than SCH may be responsible for these mild metabolic abnormalities.

Several clinical studies have reported that SCH had no significant effect on the BMI of adolescents during follow-up years [25]. However, recent reports have noted that the waist circumference and waist-to-height ratio were higher in children with SCH than in euthyroid children [11, 24]. These results suggest that children with SCH might have increased visceral adiposity, even if they have a normal degree of overall adiposity. In this study, the prevalence of abdominal obesity was 9.6% and 17.6% in euthyroid and SCH subjects, respectively. In addition, we found that the risk of abdominal obesity was two times higher in adolescents with SCH than in euthyroid adolescents after adjusting for BMI. However, some evidence suggested that elevated TSH levels might represent an adaptation of the hypothalamic–pituitary–thyroid axis to obesity [26, 27]. Elevated TSH levels in obese subjects tend to decrease with weight reduction [28, 29], suggesting that SCH may be a consequence, rather than a cause of obesity. Association studies examining SCH and obesity should therefore be interpreted with caution. Furthermore, prospective studies investigating the effects of SCH in visceral obesity are needed.

With regard to the association between BP and SCH, logistic regression analysis revealed a trend toward an

increased risk for elevated BP in SCH subjects compared with those with euthyroid, although this association was not statistically significant. Serum TSH levels also were significantly correlated with SBP after adjusting for age, sex, and BMI. We further analyzed differences in BP between non-obese euthyroid and non-obese SCH subjects to determine which metabolic effects of SCH might be unrelated to obesity. Non-obese SCH subjects had higher systolic BP compared with non-obese euthyroid subjects after adjusting for age, sex, and BMI ($P = 0.014$). This finding suggests that systolic BP was significantly correlated with SCH, independent of obesity and are consistent with those from two previous cross-sectional studies involving children and adolescents. Itterman et al. found that serum TSH levels were significantly correlated with hypertension in adolescents (OR, 1.19; $P < 0.001$) and children (OR, 1.12; $P = 0.045$) [21]. Another cohort study conducted in China found a positive correlation between TSH level and BP in adolescents [22]. However, another small study reported that BP in SCH children was not different from that in euthyroid controls, and levothyroxine treatment did not alter BP in 39 SCH subjects [30], suggesting that the association between BP and SCH in children remains unclear. Moreover, the results of these studies examining the association between SCH and BP conflict with the findings of studies involving adults. Several studies have detected positive associations, whereas others found no association [31, 32]. A possible explanation for the differing results among studies involving adolescents and adults might be that the thyroid function affects BP differently in adolescents and adults. In addition, adults are more likely than adolescents to have previous thyroid disease, hypertension, or other comorbid diseases.

This study had several limitations. First, it had a cross-sectional design; hence, no causal relationships could be determined. Second, we measured serum TSH levels at only one time point, which can lead to potential misclassifications of patients with normal thyroid function due to a transient elevation in the serum TSH level. Subjects with SCH in our study were not truly representative of a population with persistent SCH. However, the size of this dataset enabled multiple sensitivity analyses across different parameters. Third, data from KNHANES did not include some medical history, such as thyroid disease, any cancer, or chronic diseases among participants aged ≤18 years. However, the prevalence of thyroid diseases, such as hypothyroidism or hyperthyroidism, is very low in Korean adolescents (around 0.74–1.14/1,000 persons) [33], meaning these gaps in medical history are unlikely to have had a significant effect on our results.

In summary, our study found no correlation between SCH and MetS. Although it is difficult to establish a causal relationship, SCH may be associated with abdominal obesity and possibly elevated BP in adolescents. Further prospective studies are needed to confirm the relationship of SCH with MetS and its components in adolescents.

Data availability

The data that support the findings of this study are available from the KCDC database. Anybody who signs up for membership can access the raw data from the webpage.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All studies involving human participants were approved by the institutional review committee, and were performed in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent All participants signed written informed consent, and the Institutional Review Boards of the Korea National Health Insurance Service, Catholic Kwandong University College of Medicine, and International St. Mary's Hospital approved the study protocol.

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