The Frequency of Subclinical Hypothyroidism in Obese Children and Adolescents and Its Relationship with Metabolic Parameters and Atherogenic Index

Ismail Dünder, Ayşehan Akınç

Department of Pediatric Endocrinology, İnönü University, Faculty of Medicine, Malatya, Turkey

ABSTRACT

Objective: The effect of subclinical hypothyroidism on glucose and lipid metabolism in obese children is controversial. This study aims to compare cardiovascular risk factors in obese patients with or without subclinical hypothyroidism and determine the frequency of subclinical hypothyroidism in obese children and adolescents.

Materials and Methods: A total of 1130 obese children and adolescents aged 6–18 years were included in this single-center cross-sectional study. Metabolic parameters such as thyrotropin, free thyroxine, free triiodothyronine, homeostasis model assessment for insulin resistance, atherogenic index, and lipids were evaluated. The patients were divided into two groups—subclinical hypothyroidism group (free thyroxine normal, thyroid-stimulating hormone 5.5–10 mIU/L) (n = 59) and the control group (free thyroxine normal, thyroid-stimulating hormone < 5 mIU/L) (n = 1071).

Results: Subclinical hypothyroidism was detected in 59 (5.2%) of 1130 patients. The mean body mass index was similar in both groups. The mean serum insulin, homeostasis model assessment for insulin resistance, triglyceride, atherogenic index of plasma, aspartate aminotransferase, and alanine aminotransferase levels were higher in the subclinical hypothyroidism group, and the mean high-density lipoprotein cholesterol level was lower than the control group (p = .005, p < .001, p = .028, p < .001, p = .001, p < .001, and p = .018, respectively). While a positive correlation was observed between the thyroid-stimulating hormone levels and insulin, homeostasis model assessment for insulin resistance, alanine aminotransferase, triglyceride, and basal cortisol levels, a negative correlation was found between thyroid-stimulating hormone and high-density lipoprotein cholesterol.

Conclusion: Subclinical hypothyroidism can negatively affect the lipid and glucose profile.

Keywords: subclinical hypothyroidism, childhood obesity, dyslipidemia, insulin resistance, atherogenic index

INTRODUCTION

The number of overweight or obese children in the world has increased more than tenfold, from 11 million in 1975 to 124 million in 2016.¹ The longer a person is obese, the greater there is morbidity, healthcare costs, and workforce loss in adulthood.² The most common abnormality of thyroid function in obese children is isolated hyperthyrotropinemia, also known as subclinical hypothyroidism (SH), followed by minor changes in triiodothyronine (T3) and thyroxine (T4) ratios.³⁴ SH is defined as elevated serum thyroid-stimulating hormone (TSH) in the presence of normal serum total and free thyroxine (T4) levels.⁵ The prevalence of SH is 4–20% in adults and 1.5–3% in children.⁶ SH is a common finding in overweight and obese children and adolescents, with a higher prevalence in those with severe obesity and higher body mass index (BMI).⁷ The pathogenesis of SH in obese children is multifactorial, involving a combination of obesity-related endocrine and metabolic changes, hormonal imbalances, and increased cytokine levels.

Corresponding author:
Ismail Dünder
isdismail_dundar@yahoo.com
Received: September 20, 2021
Accepted: December 30, 2021

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Cite this article as: Dünder I, Akınç A. The frequency of subclinical hypothyroidism in obese children and adolescents and its relationship with metabolic parameters and atherogenic index. Turk Arch Pediatr. 2022;57(3):316–322.
children with a 7–36% rate. There are several factors associated with SH, such as chronic lymphocytic thyroiditis, iodine deficiency, medications, gene defects, genetic syndromes, and obesity. It has been hypothesized that the increase in TSH concentrations in obesity may represent a mechanism aimed at increasing energy expenditure. In this context, the existence of an adipose tissue–hypothalamus–pituitary–thyroid axis has been suggested. This model claims that leptin secreted by adipocytes affects communication between adipocytes and the hypothalamus by increasing the secretion of thyrotropin-releasing hormone (TRH) and TSH and the peripheral conversion of T4 to T3.

Some studies have identified SH as an essential risk factor for developing and progressing cardiovascular disease, insulin resistance, and non-alcoholic fatty liver disease (NAFLD) in obese children and adolescents. In a study conducted with obese children and adolescents, Aeberli et al showed that TSH levels were significantly correlated with total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), insulin, and homeostasis model assessment for insulin ratio (HOMA-IR). Despite uncertainty about the underlying mechanism, the finding that abnormalities in thyroid function mostly normalize after weight loss supports the hypothesis that TSH elevation in obese patients is reversible and is a consequence rather than a cause of obesity. The prevalence of SH in Turkish obese children and adolescents was reported in the range of 9.2–36%. The prevalence of SH is high in obese children, and the necessity of L-thyroxine therapy is still an important debate.

Therefore, the aim of the present study was (1) to determine the frequency of SH in obese children and adolescents, (2) to investigate the relationship between high TSH levels and various anthropometric measurements (body mass index, body mass index standard deviation score, waist/hip ratio), atherogenic index, and metabolic parameters (lipid profile and insulin resistance) in these children.

MATERIALS AND METHODS

Study Population
This study was performed in the Pediatric Endocrinology Department of İnönü University Hospital. A total of 1130 obese children 6–18 years of age who had been brought to the outpatient clinic were consecutively recruited for the study from March 2013 to September 2017. Our study is a single-center and cross-sectional study. Inclusion criteria for the study were: (1) an age range of 6–18, (2) a BMI greater than the 95th percentile for age and gender, (3) absence of a prior major illness. Exclusion criteria were: (1) patients with overt hypothyroidism (excluding SH), patients with chronic lymphocytic thyroiditis, patients with Cushing’s syndrome, patients receiving thyroid hormone, and patients receiving topical or systemic glucocorticoid medication; (2) cases with familial dyslipidemia; (3) patients with syndromic, monogenic, and secondary obesity; and (4) patients with TSH levels >10 IU/mL. Hospital records of the cases were reviewed retrospectively. The patients were divided into two groups according to the thyroid function test results. Subjects with normal fT4 levels and 5.5–10 mIU/L TSH levels were included in the SH group.

The control group consisted of subjects with normal fT4 levels and TSH levels of <5.5 mIU/L. Both groups were compared in fasting plasma glucose, insulin, HOMA-IR, lipid profile, and other metabolic parameters.

Ethical Approval
Ethics Committee Approval: The study proposal was approved by the Ethics Committee of İnönü University Faculty of Medicine (Approval Number: 2020-155). Since the study was performed retrospectively, patient informed consent forms were not needed.

Anthropometric Examination
A complete physical examination, including anthropometric measurements, was performed on each child. Puberty development was assessed according to Tanner staging. A testicular volume of 4 mL or more in males and ≥2 breast development in females according to Tanner’s staging were accepted as signs indicating the onset of puberty. Anthropic measurements were performed in the morning, following an overnight fast, without street clothes and shoes. A Harpenden stadiometer (with a sensitivity of 0.1 cm) was used for height measurement. Weight measurement was performed via the BMI SECA scale (with a sensitivity of 0.1 kg). BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured at the level of the umbilicus while standing and breathing regularly, hip circumference was measured at the level of the iliac crest, and blood pressure was measured by a standard mercury sphygmomanometer after at least 10 minutes of rest.

Laboratory Measurements
Hypertension and systolic blood pressure were accepted as above the 95th percentile for age and gender. Insulin resistance was defined using the HOMA-IR using the following standard formula: [fasting insulin (mIU/mL) × fasting glucose (mmol/L)/22.5]. Insulin resistance was defined as a HOMA-IR >2.5 in prepubertal children and >3.16 in pubertal children. Samples were taken for at least 12–14 hours post-fasting, and blood glucose (FBC), lipid profile (HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TC: total cholesterol, TG: triglyceride), and insulin levels were measured. Serum TC levels >200 mg/dL, triglyceride (TG) levels >150 mg/dL, LDL-C levels >130 mg/dL, or HDL-C levels <40 mg/dL were accepted as dyslipidemia. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) normal values were set below 41 U/L and 37 U/L, respectively. With basal cortisol enzyme immunoassay kits, the normal level was taken as 3–21 μg/dL.

Fasting insulin, TSH, and fT4 levels were studied with two-chamber two-step enzymatic immunoassay methods using a Beckman Coulter Dxi 800 device. According to reference values of Beckmann Coulter TSH and fT4 kits used in our hospital laboratories, TSH low and high limit values were set as 0.35–5.5 mIU/mL, and fT4 low and high limit values were set as 0.61–1.32 ng/dL. The fT3 normal range is given in the range of 1.9–4.2 pg/mL. SH is defined as an elevated serum TSH concentration ≥5.5 IU/mL (97.5th for our assay) in the presence of normal serum fT4. The glucose oxidase method for blood glucose measurement and Olympus AU 2700 were used.
for lipid measurement. Insulin levels were measured by electrochemiluminescence method on Roche Modular Analytics E-170 immunoassay analyzer (Roche Diagnostics, USA). The atherogenic index of plasma (AIP) was calculated as the logarithm of the molar ratio of triglyceride to high-density lipoprotein cholesterol (TG/HDL-C). AIP was classified as <0.11 as low risk, 0.11–0.21 as intermediate risk, and >0.21 as increased risk.28 Upper abdominal ultrasonographic examination was performed to diagnose hepatosteatosis using the GE LOGIC S8, USA, ultrasound device. Liver ultrasound findings were listed as follows: normal liver appearance (no hepatosteatosis), mild (stage 1), moderate (stage 2), and severe hepatosteatosis (stage 3).28

**Statistical Analysis**

Statistical analysis was performed using the statistical Package for the Social Sciences Statistics 15.0 (SPSS Inc.; Chicago, IL, USA) program package. Categorical variables were analyzed using the chi-square test. The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. The Student's t-test and the Mann-Whitney U-test were used for the comparison of groups according to the parametric values. For correlation analyses, the Pearson test was used for the parametric variables and the Spearman test was used for the nonparametric variables. A P value <.05 was accepted as statistically significant.

**RESULTS**

**Clinical Characteristics of the Subjects**

A total of 1130 obese cases (526 girls (46.4%) and 604 boys (53.6%)) were included in the study. The mean age of the patients was 10.9 ± 3.6 years, and 638 (56.5%) cases were pubertal. Demographic characteristics and laboratory data of the patients are shown in Table 1. Demographic and laboratory values of the patients according to puberty status are shown in Table 2.

**Comparison of Anthropometric and Laboratory Parameters Between SH (+) and SH (−) Groups**

SH was determined in a total of 59 patients (5.2%). There were 1071 patients (94.8%) in the control group whose thyroid function test results were normal. No difference was found between the groups concerning sex distribution (P = .503). The puberty status was similar in both groups (P = .224). While the mean BMI SDS was 2.2 ± 0.3 in the SH group, it was 2.2 ± 0.4 in the control group. Both groups were similar concerning BMI SDS (P = .290). When groups were compared on glucose metabolism, the fasting insulin, IR, and the HOMA-IR levels were higher in the SH group (P < .005, P < .001, and P < .001, respectively). When the groups were compared concerning lipid metabolism, while the HDL-C level was lower, the TG level was higher in the SH group than the control group (P = .018, P = .028, respectively).

---

**Table 1. Distribution of Patients’ Demographic Characteristics and Laboratory Findings by Gender**

| Total | Female | Male | P |
|-------|--------|------|---|
| n (%) | 1130 (100) | 526 (46.5) | 604 (53.5) | NS |
| Age (yr) | 10.9 ± 3.6 | 11.5 ± 3.1 | 11.3 ± 2.9 | NS |
| BMI SDS | 2.2 ± 0.4 | 2.1 ± 0.3 | 2.3 ± 0.4 | <.001<sup>a</sup> |
| Fasting glucose (mg/dL) | 89.2 ± 8.1 | 88.1 ± 7.7 | 90.1 ± 8.3 | <.001<sup>a</sup> |
| Fasting insulin (μIU/mL) | 18.3 ± 11.3 | 18.9 ± 11.7 | 17.7 ± 9 | NS<sup>b</sup> |
| HOMA-IR | 4.0 ± 2.3 | 4.1 ± 2.5 | 3.9 ± 2.2 | NS<sup>b</sup> |
| Total cholesterol (mg/dL) | 167.2 ± 33.1 | 165.6 ± 30.8 | 168 ± 34.8 | NS<sup>b</sup> |
| Triglycerides (mg/dL) | 122.9 ± 62.8 | 122.1 ± 59.8 | 123.5 ± 65.1 | NS<sup>b</sup> |
| LDL-C (mg/dL) | 100.2 ± 28.9 | 99.5 ± 27.2 | 100.7 ± 30.1 | NS<sup>b</sup> |
| HDL-C (mg/dL) | 44.0 ± 11.8 | 44.2 ± 12.2 | 43.8 ± 11.5 | NS<sup>b</sup> |
| Waist-to-hip ratio | 0.95±0.03 | 0.94 ± 0.03 | 0.96 ± 0.03 | <.001<sup>b</sup> |
| FT3 (pg/mL) | 5.1 ± 1.2 | 5.1 ± 1.3 | 5.1 ± 1.1 | NS<sup>b</sup> |
| FT4 (ng/dL) | 1.03 ± 0.2 | 1.03 ± 0.2 | 1.03 ± 0.2 | NS<sup>b</sup> |
| TSH (mIU/mL) | 2.84 ± 1.3 | 2.8 ± 1.4 | 2.8 ± 1.2 | NS<sup>b</sup> |
| SH, % (n) | 5.2 (59) | 6.5 (34) | 4.1 (25) | NS<sup>b</sup> |
| Insulin resistance, %, (n) | 54.2 (512) | 50.8 (267) | 57.1 (345) | .019<sup>a</sup> |
| Hypertension, %, (n) | 18.2 (206) | 19.2 (101) | 17.4 (105) | NS<sup>b</sup> |
| Dyslipidemia, %, (n) | 56.5 (639) | 54.4 (286) | 58.4 (353) | NS<sup>b</sup> |
| -Hypercholesterolemia, %, (n) | 15.9 (180) | 14.4 (76) | 17.2 (104) | NS<sup>b</sup> |
| -Hypertriglyceridemia, %, (n) | 25.9 (293) | 25.9 (136) | 26 (157) | NS<sup>b</sup> |
| -High LDL-C level, %, (n) | 14.6 (165) | 14.6 (77) | 14.6 (88) | NS<sup>b</sup> |
| -Low HDL level, % | 36.7 (415) | 35.9 (189) | 37.4 (226) | NS<sup>b</sup> |
| Hepatosteatosis, %, (n) | 44.1 (499) | 36.9 (195) | 49.7 (304) | <.001<sup>c</sup> |
| -Grade 1, %, (n) | 38.6 (436) | 33.8 (178) | 42.7 (258) | |
| -Grades 2–3, %, (n) | 5.6 (63) | 3.2 (17) | 7.6 (46) | |

BMI SDS: body mass index standard deviation score, HOMA-IR: homeostasis model assessment of insulin resistance, HDL: high-density lipoprotein, LDL: low-density lipoprotein, FT4: free thyroxine, FT3: free triiodothyronine, TSH: thyroid-stimulating hormone, SH: subclinical hypothyroidism, NS: not significant.

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

<sup>a</sup>Independent samples t-test. <sup>b</sup>Mann-Whitney U-test. <sup>c</sup>Chi-square test.

Boldface indicates a statistically significant difference with P < .05.
respectively). Anthropometric and laboratory measurements of both groups are summarized in Table 3.

**Table 2.** Distribution of Patients’ Demographic Characteristics and Laboratory Findings According to Pubertal Status

|                | Prepubertal | Pubertal | P        |
|----------------|-------------|----------|----------|
| n (%)          | 492 (43.5)  | 638 (56.5)|         |
| Age (yr)       | 8.7 ± 1.7   | 13.1 ± 2.2| <.001a   |
| BMI SDS        | 2.3 ± 0.5   | 2.1 ± 0.3 | <.001b   |
| Fasting insulin (µIU/mL) | 14.1 ± 10.6 | 21.5 ± 10.7 | <.001c   |
| Fasting glucose (mg/dL) | 89.1 ± 8.3  | 89.3 ± 7.9  | NSc      |
| HOMA-IR        | 3.04 ± 1.9  | 4.7 ± 2.4 | <.001a   |
| Total cholesterol (mg/dL) | 167.5 ± 32.5 | 166.9 ± 33.5 | NSb      |
| Triglycerides (mg/dL) | 125.5 ± 56.3 | 131.0 ± 66.2 | <.001a   |
| LDL-C (mg/dL)  | 100.6 ± 27.6| 100.0 ± 29.7| NSb     |
| HDL-C (mg/dL)  | 45.9 ± 12.5 | 42.6 ± 11.0| <.001a   |
| Waist-to-hip ratio | 0.96 ± 0.02 | 0.94 ± 0.03 | <.001c   |
| SH, % (n)      | 5.9 (29)    | 4.7 (30)  | NSc      |
| Insulin resistance, % (n) | 49.8 (245) | 57.7 (367) | .006b    |
| Hypertension, % (n) | 14.2 (70)   | 21.3 (136) | <.001a   |
| Dyslipidemia, % (n) | 49.4 (243) | 61.1 (396) | <.001a   |
| • Hypercholesterolemia, % (n) | 16.7 (82)  | 15.4 (94)  | NSc      |
| • Hypertriglyceridemia, % (n) | 20.9 (68)   | 29.8 (97)  | <.001a   |
| • High LDL-C level, % (n) | 13.8 (103)  | 15.2 (190) | NSb      |
| • Low HDL level, % (n) | 28.5 (140)  | 43.1 (275) | <.001a   |
| Hepatosteatosis % (n) | 37.4 (184)  | 49.2 (315) | <.001b   |
| • Grade 1, % (n) | 33.9 (167)  | 42.2 (269) |         |
| • Grades 2–3, % (n) | 3.5 (17)    | 7.2 (46)   |         |

Values are presented as number (%) or mean ± standard deviation. BMI SDS: body mass index standard deviation score, HOMA-IR: homeostasis model assessment of insulin resistance, HDL: high-density lipoprotein, LDL: low-density lipoprotein, SH: subclinical hypothyroidism, NS: Not significant.

*Independent samples t-test. †Mann-Whitney U-test. ‡Chi-square test. Boldface indicates a statistically significant difference with P < .05.

**Correlations Between TSH and Metabolic Parameters**

There was a positive correlation between TSH levels and some metabolic parameters, such as insulin (r = .19, P < .001), HOMA-IR (r = .16, P < .001), ALT (r = .06, P = .028), glucose (r = .07, P = .019), Cortisol (r = .12, P < .001), and TG (0.17, P < .001). A negative correlation was found between TSH level and HDL-C (r = −.03, P = .005). There was no correlation between TSH level and BMI, SDS and AST. The correlation between TSH and metabolic parameters is shown in Figure 1.

**DISCUSSION**

In this study, the relationship between SH and metabolic parameters in obese children and adolescents was evaluated. SH was found in 5.2% of 1130 obese children and adolescents. Fasting insulin, HOMA-IR, basal cortisol, ALT, and TG levels were higher in the SH group, while HDL-C was lower. In addition, there was a positive correlation between TSH levels and fasting insulin, HOMA-IR, fasting glucose, basal cortisol, ALT, and TG levels, while a negative correlation was found with HDL-C levels.

The most common thyroid disorder in obese children and adolescents is increased serum TSH and FT3 levels. This increase in TSH (and therefore T3) can be interpreted as a defense mechanism of the body against weight gain. Conversion of T4 to T3 is increased in obese individuals as a result of increased deiodinase activity due to fat deposition. In our study, no significant difference was found between SH (+) and SH (−) subjects in terms of FT3 or FT4 levels. However, while FT4 levels were within the normal range in both groups, FT3 levels were above the normal range. In the light of this information, the fact that FT4 is within normal limits and FT3 levels are increased in obese patients can be explained by this mechanism.

The prevalence of SH in obese children and adolescents has been reported in the range of 7%–36%. This can be explained by differences in ethnicity, geographical region,
Figure 1. Correlation between thyrotropin (TSH) and fasting insulin, homeostasis model assessment for insulin resistance (HOMA-IR), ALT, triglyceride, fasting glucose, and basal cortisol in obese patients. TSH, thyroid-stimulating hormone, HOMA-IR: homeostasis model assessment of insulin resistance, ALT, alanine aminotransferase
and cut-off values for TSH. Thyroid hormones play a role in basal metabolism and energy expenditure. Therefore, interest in the relationship between thyroid functions and obesity has increased.\cite{32,33} There are studies in the literature showing a positive correlation between TSH and BMI.\cite{11,17} In our study, however, we did not find a correlation between TSH levels and BMI. No relationship was observed between TSH levels and gender or puberty status.\cite{8,11} Dahl et al.\cite{31} found higher TSH levels in boys than girls in a study conducted with 1796 obese/overweight subjects during childhood and adolescence. In our study, no difference was found between the groups with and without SH regarding age, gender, and pubertal status.

Thyroid hormones play an important role in glucose metabolism. Significant hypothyroidism is associated with obesity, insulin resistance, hyperglycemia, dyslipidemia, and increased cardiovascular events.\cite{31} The effect of thyroid functions on metabolic parameters is discussed because of the higher prevalence of SH in obese patients than non-obese patients. Many studies investigate the relationship between thyroid hormones and glucose and lipid metabolism in obese children and adolescents.\cite{8,11,30,32} While some studies reported an association between TSH and insulin and HOMA-IR, some studies have not reported such an association.\cite{8,11,15} In our study, insulin and HOMA-IR values were higher in the SH group. In addition, a positive correlation was found between TSH levels and insulin and the HOMA-IR index.

In our study, basal cortisol levels were within normal limits in both groups, and cortisol levels were higher in the SH group than in the group without SH. In our study, we found a significant positive correlation between TSH and basal cortisol levels. Walter et al.\cite{33} reported a positive correlation between TSH and cortisol in their study. The increase in cortisol in parallel with the increase in TSH can be explained by decreased cortisol clearance and negative feedback in the blunted hypothalamic–pituitary–adrenal axis. Nevertheless, important questions such as whether this relationship is pathological or physiological and other mechanisms involved in this relationship still remain.

Some limitations of the study are that (1) it was designed retrospectively; (2) there was no control group including children and adolescents with normal weight; (3) the iodine status of obese children and genetic causes of SH were not investigated.

CONCLUSIONS

Despite its limitations, risk factors for cardiovascular disease (CVD) (high atherogenic index, insulin resistance, HOMA-IR, TG level, and low HDL-C level) were significantly higher in patients with SH in this study, which compared obese children and adolescents with similar BMI, without including patients with autoimmune thyroid disease in the study. Increased TSH can negatively affect the lipid and glucose profile. As a result, larger prospective studies with an increasing number of cases in each group are needed to investigate the relationship between SH and metabolic changes in obese children and adolescents with SH.

REFERENCES

1. NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017;390(10131):2627-2642. [CrossRef]
2. Hamilton D, Dee A, Perry L. The lifetime costs of overweight and obesity in childhood and adolescence: a systematic review. Obes Rev. 2018;19(4):452-463. [CrossRef]
3. Fontenelle LC, Feitosa MM, Severo JS, et al. Thyroid function in human obesity: underlying mechanisms. Horm Metab Res. 2016;48(12):787-794. [CrossRef]
4. Yadav J, Jain N, Dayal D. Alterations of thyroid function in overweight and obese children: an update. Indian J Child Health. 2018;5(3):145–150. [CrossRef]

5. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29(1):76–131. [CrossRef]

6. Salerno M, Capalbo D, Cerbone M, De Luca F. Subclinical hypothyroidism in childhood - current knowledge and open issues. Nat Rev Endocrinol. 2016;12(12):734–746. [CrossRef]

7. Pacifico L, Anania C, Ferraro F, Andreoli GM, Chiesa C. Thyroid function in childhood obesity and metabolic comorbidity. Clin Chim Acta. 2012;413(3-4):396–405. [CrossRef]

8. Kara O. Influence of subclinical hypothyroidism on metabolic parameters in obese children and adolescents. Clin Exp Pediatr. 2020;63(3):110–114. [CrossRef]

9. Çelik N. The prevalence of subclinical hypothyroidism in obese children and adolescents and its effects on metabolic parameters. Cumhuriyet Tip Derg. 2019;41(4):691–697. [CrossRef]

10. Andler W. Thyroid hormones and their relation to weight status. Horm Res. 2008;70(1):51–57. [CrossRef]

11. Reinehr T, Isa A, De Sousa G, Dieffenbach R, Andler W. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

12. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

13. Maratou E, Hadjidakis DJ, Kollias A, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–790. [CrossRef]

14. Reinehr T, Isa A, Murer SB, et al. Thyroid function derangement and childhood obesity: an Italian experience. BMC Endocr Disord. 2010;10(1):8. [CrossRef]

15. Aeberli I, Jung A, Murer SB, et al. During rapid weight loss in obese children and adolescents METABOLIC. 2010;95(12):5412–5418. [CrossRef]

16. Maratou E, Hadjidakis DJ, Kollias A, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–790. [CrossRef]

17. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

18. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

19. Maratou E, Hadjidakis DJ, Kollias A, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–790. [CrossRef]

20. Aeberli I, Jung A, Murer SB, et al. During rapid weight loss in obese children, reductions in TSH predict improvements in insulin sensitivity independent of changes in body weight or fat. J Clin Endocrinol Metab. 2010;95(12):5412–5418. [CrossRef]

21. Wollers B, Loss N, Reinehr T. TSH and free triiodothyronine concentrations are associated with weight loss in a lifestyle intervention study. Pediatr Obes. 2016;11(12):734–746. [CrossRef]

22. Holmes DT, Frohlich J, Buhr KA. The concept of precision extended to the atherogenic index of plasma. Clin Biochem. 2008;41(7-8):631–635. [CrossRef]

23. Scatari O, Scott W, Donovan P, Siegelman SS, Sanders RC. Fatty infiltration of the liver: ultrasonographic and computed tomographic correlation. J Ultrasound Med. 1984;3(1):9–14. [CrossRef]

24. Reinehr T. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

25. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

26. Holmes DT, Frohlich J, Buhr KA. The concept of precision extended to the atherogenic index of plasma. Clin Biochem. 2008;41(7-8):631–635. [CrossRef]

27. Holmes DT, Frohlich J, Buhr KA. The concept of precision extended to the atherogenic index of plasma. Clin Biochem. 2008;41(7-8):631–635. [CrossRef]

28. Scatari O, Scott W, Donovan P, Siegelman SS, Sanders RC. Fatty infiltration of the liver: ultrasonographic and computed tomographic correlation. J Ultrasound Med. 1984;3(1):9–14. [CrossRef]

29. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

30. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

31. Maratou E, Hadjidakis DJ, Kollias A, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–790. [CrossRef]

32. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

33. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

34. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

35. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

36. Maratou E, Hadjidakis DJ, Kollias A, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–790. [CrossRef]

37. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

38. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

39. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

40. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

41. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

42. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

43. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

44. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

45. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

46. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

47. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]

48. Yavuz S, Salgado Nunez Del Prado S, Celi FS. Thyroid hormone action and energy expenditure. J Endocr Soc. 2019;3(7):1345–1356. [CrossRef]

49. Reinehr T, Isa A, Murer SB, et al. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr. 2011;23(4):415–420. [CrossRef]