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Associations between adiposity and indicators of thyroid status in children and adolescents

Amanda J. Krause[1,2], **Brittany Cines**[1], **Elizabeth Pogrebniak**[1], **Roya Sherafat-Kazemzadeh**[1], **Andrew P. Demidowich**[1], **Ovidiu A. Galescu**[1], **Sheila M. Brady**[1], **James C. Reynolds**[3], **Van S. Hubbard**[2], and **Jack A. Yanovski**[1]

[1]Section on Growth and Obesity, Program in Developmental Endocrinology and Genetics, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), National Institutes of Health (NIH)

[2]NIH Division of Nutrition Research Coordination, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH

[3]Division of Nuclear Medicine, Radiology and Imaging Sciences Department, Hatfield Clinical Center, NIH

Abstract

Background—In adults, obesity is associated with abnormalities of thyroid function; there are fewer studies in pediatric cohorts.

Objectives—To examine associations of weight and adiposity with indices of thyroid function and thyroid-related metabolic factors in children.

Design/Methods—A sample of 1203 children without obesity (BMI<95th percentile; n=631) and with obesity (BMI≥95th percentile; n=572), age 5-18y, had height and weight measured (to calculate BMI-Z score for age and sex) and had blood collected in the morning for thyroid-stimulating hormone (TSH), free thyroxine (FT4), and leptin. A subset (n=829) also underwent measurement of fat mass by dual-energy x-ray absorptiometry. Analyses examined associations of TSH and FT4 with adiposity and obesity-related conditions, accounting for sociodemographic factors.

Results—TSH was positively related to BMIz and fat mass (both p-values <.001). FT4 was negatively related to BMIz and fat mass (both p-values <.001). TSH was positively correlated to leptin (p=.001) even after accounting for fat mass.

Conclusions—Pediatric obesity is associated with higher TSH and lower FT4 concentrations and with a greater prevalence of abnormally high TSH. Leptin concentrations may in part explain obesity's effects on thyroid status, perhaps through leptin's effects on TSH secretion.

Correspondence to: Jack A. Yanovski, M.D., Ph.D., Chief, Section on Growth and Obesity, PDEGEN, NICHD, National Institutes of Health, 10 Center Drive, Hatfield Clinical Research Center, Rm 1E-3330, MSC 1103, Bethesda, Maryland 20892-1103, Phone: 301-496-0858; Fax: 301-402-0574; jy15i@nih.gov.

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Keywords

thyrotropin; thyroid stimulating hormone; free thyroxine; overweight; obesity; fat mass; child; adolescent; pediatric; TSH; subclinical hypothyroidism

Introduction

Many studies in adults have examined the relationship between high body adiposity or BMI and abnormal thyroid function (1–5) (see also Online Supporting Information). Low thyroid hormone is associated with reduced energy expenditures (6) and fluid retention (7) in adults with overt hypothyroidism. However, less severe hypothyroidism does not appear to induce greater body fatness or weight, since l-thyroxine replacement leads to relatively small changes in body composition (8, 9). Elevated thyroid stimulating hormone (TSH) that does not exceed 2.5 times the upper limit of the normal range in association with a normal free thyroxine (FT4) concentration, referred to as “subclinical hypothyroidism,” is frequently observed in adults with obesity who have no evidence of autoimmune thyroiditis (10). Obesity-associated subclinical hypothyroidism may be a consequence, rather than a cause of obesity because the hyperthyrotropinemia appears to remit after weight loss (11).

In some studies of euthyroid adults with obesity, high adiposity is associated with increased TSH (2–5) and free or total triiodothyronine (T3) (2, 3, 5) and mildly decreased free thyroxine (FT4) (5). However, the data are inconsistent; other studies have not found an association between measures of adiposity and TSH (12–14), T3 (4, 12, 13), or FT4 (2–4, 12, 14). There have been fewer studies in pediatric cohorts; most of these studies have had relatively small sample sizes (15–21), and also reported inconsistent results. The majority of papers found an association between TSH and BMI (17–19, 22, 23), as well as between T3 and BMI (16–19, 22, 23) but others have not (15). Contrary to most research in adults, there was no association between FT4 and BMI found in the majority of pediatric studies (15–20, 22, 23).

Additionally, among obese children, the association of thyroid hormone concentrations with serum leptin and other metabolic parameters is unclear. Leptin, a hormone produced by adipocytes, regulates energy homeostasis and neuroendocrine and behavioral responses to overfeeding, and has been hypothesized to contribute to the altered thyroid status observed in obesity (1). Some studies have found leptin to be positively associated with TSH (1, 12, 15) and negatively related to FT4 (12) in both adults and children, but other investigations have not (16). Similarly, research into the relationship between thyroid status and lipid profile, even when controlling for adiposity measures, has been mixed, with some (15, 24), but not all studies (4, 22) demonstrating that lipid profile components are associated with FT4 or TSH.

The main objective of this investigation was to clarify the conflicting data for the relationship between measures of adiposity with TSH and FT4 in a large pediatric cohort containing substantial numbers of children and adolescents with obesity. We hypothesized that adiposity would be positively associated with TSH and negatively associated with FT4 among a mixed cohort of children with- and without obesity, but that these associations

might differ when those with- and without obesity, or when younger (age <10y) and older (≥10y) subsamples, were examined separately. We also sought to clarify the relationships between thyroid status and both leptin and aspects of the lipid profile.

Subjects and Methods

A convenience sample was assembled from 10 pediatric studies at the National Institutes of Child Health and Human Development (NICHD) conducted between June 1996 and June 2014 that recruited generally-healthy children. Some were non-overweight but by design, the cohort oversampled for children with overweight or obesity. Additional information about the studies contributing to the sample and study procedures are reported in Online Supporting Information.

Morning (8:00am-10:00am) fasting TSH, FT4, lipid profiles including triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and total cholesterol (TC), and leptin were measured. FT4 and TSH were measured by a homogenous, sequential, chemiluminescent immunoassay based on LOCI® technology, using the Siemens Healthcare Dimension Vista® System (Dade Behring Inc.) See Online Supporting Information for additional assay details.

SPSS 18.0 for Windows (SPSS Inc., Chicago, IL) was used for statistical analyses. Log transformations were applied to normalize TG and HDL-C. FT4 was square root transformed based off the Levene's Test of Equality of Error Variances. Following transformations, TG and HDL-C were normal; however, the p value for the square root transformed FT4 was still significant, but less so than with any other transformation. Leptin in both spreadsheets could not be normalized, and thus had statistically different values in the Levene's Test of Equality of Error Variances. ANCOVA was used to examine associations of BMI z-score (BMIz) or Fat Mass (kg) with TSH and FT4 adjusting for age, SES, sex, race, and puberty stage, plus height (m) for Fat Mass. Analyses were conducted in this manner for the entire population, with secondary analyses carried out specifically for participants <10y, ≥10y (to correspond to prior analyses) (10, 16, 18, 20, 22). An ANCOVA analysis controlling for age, SES, puberty stage, race, and sex was run to compare the 3 categories for BMI status: non-overweight (BMIz<1.036), overweight (BMIz 1.036-1.644), and obesity (BMIz ≥1.645). With these same control variables, analyses were run to compare associations of TSH and FT4 with leptin, TC, LDL-C, HDL-C, and TG as dependent variables. To determine if sample characteristics for those with missing data differed, ANCOVA controlling for sex, race, SES, age, and puberty stage were run to compare associations of BMIz or fat mass (kg) with TC, LDL-C, HDL-C, and TG. T-tests comparing excluded participants to the participants included in analyses for the categories of SES, age, weight, height, BMI, and BMIz for the BMI sample; and SES, age, weight, height, fat mass, and percent fat for the DXA sample. Race and sex for excluded and included participants were compared by contingency table analysis. Based on conducting 4 main analyses (BMIz and Fat Mass versus TSH and FT4), the p-values considered significant for these main ANCOVAS were adjusted to p≤0.0125.

Results

BMI Analyses

From a total of 1,376 available participants, 173 were excluded (159 missing data, 11 taking levothyroxine, and 3 with TSH ≥12uIU/mL), leaving a total of 1,203 with measured TSH of whom 955 also had measured FT4. Sample characteristics for included participants are presented in Table 1A. There were 787 females and 416 males, 461 (38.3%) non-Hispanic Blacks (NHB), and 640 (53.2%) non-Hispanic Whites (NHW). The "other" racial category comprised 37 Asians, 1 American Indian/Alaskan Native, 23 Hispanics, and 41 multi-racial individuals. Nearly half of the sample, 572 (47.5%), had BMI ≥95th percentile, and 488 (40.6%) participants had BMI ≥97th percentile. When comparing the excluded and included samples, there were no significant differences in SES, age, weight, height, BMIz, or sex; however, with regard to race, there were a greater percentage of NHB (43.4%) and a lower percentage of NHW (42.2%) in the excluded than the included group (p=.006).

For the full sample, ANCOVA analyses with SES, sex, race, puberty stage, BMIz, and age in the model (Table 2) found a positive relationship between BMIz and TSH (p<.001; Supplemental Figure 1A). BMIz was negatively associated with FT4 (p<.001; Table 2; Supplemental Figure 1B) as were SES (p<.001) and age (p<.001). The proportion of children with high TSH consistent with subclinical hypothyroidism (TSH 4.5-10 uIU/mL) was greater among children with vs. without obesity (4.8 vs. 1.6%, p<0.001). We also found that prepubertal children had a higher FT4 than mid-pubertal children (p=.003); however, there were no significant differences between prepubertal and late-pubertal or mid-pubertal and late-pubertal children. In the BMIz ANCOVA (Table 2), there were no significant sex, age, SES, or puberty stage effects with TSH as the dependent variable, and no significant effects for sex or race with FT4 as the dependent variable. In the entire population we also examined the associations of TSH or FT4 with leptin, TC, LDL-C, HDL-C, and TG after accounting for BMI. TSH was positively related to TG (ß±SEM .028±.005, p<.001) and FT4 was negatively related to TG (ß±SEM -.259±.078, p=.001). No significant relationships were found between TSH or FT4 and leptin, TC, LDL-C, or HDL-C after BMI was taken into account.

Among participants <10y, BMIz was positively associated with TSH (ß±SEM .146±.049, p=.003; N=360), but not significantly associated with FT4 (p=.289; N=359). In participants ≥10y with TSH (N=832) or FT4 (N=587) as the dependent variable, a positive relationship was found between BMIz and TSH (ß±SEM .164±.036, p<.001) and a negative relationship with FT4 (ß±SEM -.017±.003, p<.001).

Examining BMI categorically split into non-overweight, overweight, and obesity groups, children with obesity had higher TSH than both non-overweight (ß±SEM .430±.072, p<.001), and overweight children (.213±.091, p=.019), and a lower FT4 than children who were not overweight (ß±SEM -.030±.006, p<.001). Children who were overweight had higher TSH than non-overweight children (.217±.094, p=.021) and a lower FT4 than children who were not overweight (-.027±.009, p=.003).

DXA Analysis

From a total of 1,002 available participants, 173 were excluded (169 missing data and 4 patients taking levothyroxine), leaving a total of 829 participants with measured TSH of whom 714 also had measured FT4. Sample characteristics for included participants are presented in Table 1B. There were 576 females and 253 males, 340 (41.0%) NHB, and 422 (50.9%) NHW. The “other” racial category comprised 23 Asians, 1 American Indian or Alaskan Native, 17 Hispanics, and 26 multi-racial individuals. When comparing the excluded and included samples, there were no significant differences in SES, BMI, BMIz, fat mass, percent fat, or sex; however, significant differences were found between age (p=.001), height (p<.001), weight (p=.007) and race (p=.018). The average age in the excluded group was 11.6 compared to 12.5 years old in the included group. The excluded group was taller (149.2 vs. 154.1cm), lighter (62.7 vs. 69.6 kg) and had a greater percentage of NHB (42.2%) and a lower percentage of NHW (43.4%) than the included group.

ANCOVA analyses with sex, race, puberty stage, age, SES, height, and fat mass in the model (Table 3) found fat mass was positively correlated with TSH (p<.001, Supplemental Figure 1C) and negatively correlated with FT4 (p<.001; Supplemental Figure 1D). NHB were found to have a lower TSH than NHW (ß±SEM, p −.222±.082, p=.007). In the fat mass model (Table 3), there were no significant sex, pubertal stage, age, SES, or height effects with TSH as the dependent variable, and no significant sex, race, puberty stage, age, SES, or height effects with FT4 as the dependent variable. In the fat mass sample, we also examined associations of TSH or FT4 with leptin, TC, LDL-C, HDL-C, and TG. After accounting for fat mass, TSH was positively associated with leptin (ß±SEM 1.237±.365, p=.001) and TG (ß ±SEM .025±007, p<.001); FT4 was negatively associated with TG (ß±SEM -.128±.040, p=.001).

Among participants <10y, fat mass was positively associated with TSH (ß±SEM .023±.009, p=.016; N=216), and negatively associated with FT4 (ß±SEM -.004±.002, p=.012; N=216). In participants ≥10y, fat mass was positively associated with TSH (ß±SEM .009±.003, p=.002; N=602), and negatively associated with FT4 (ß±SEM -.001±.001, p=.021; N=489).

Discussion

In a large pediatric cohort of participants with and without obesity, we found that measures of adiposity, including BMIz and fat mass, had a significant positive relationship with TSH and a negative relationship with FT4, although adiposity explained only a small fraction of the variance of TSH and FT4. Both BMIz and fat mass were positively associated with TSH in both children <10y and ≥10y and negatively associated with FT4 in children ≥10y. Among children <10y, we found no significant association between BMIz and FT4, although fat mass was negatively associated with FT4. Most lipid measurements were not significantly related to either TSH or FT4, but there was a positive association between TSH and TG, and a negative association between FT4 and TG.

In this study we confirmed the positive correlation between measures of adiposity and TSH, which has been previously reported in both adults (2–5), and children (17–19, 22, 23). In both BMI and DXA cohorts, we also confirmed the significant negative relationship between

measures of adiposity and FT4, which has been observed in somewhat fewer studies (5, 25). We additionally examined participants split into two age categories because the negative relationship between measures of adiposity and FT4 was less commonly reported in younger pediatric samples. As many of the pediatric studies in the literature include mean ages <10y (10, 16, 18, 20, 22), we used 10y as the cut point between groups. As expected, adiposity measures remained positively associated with TSH in both the <10y and ≥10y groups. However, among children <10y, a significant negative relationship between BMIz and FT4 was not found. One possible explanation for finding a BMIz-FT4 relationship only among adolescents might be that subclinical autoimmune thyroiditis is more prevalent among adolescents and exacerbated obesity-related findings. However, the reversibility of thyroid abnormalities with weight loss that has previously been described in adolescents (26) is not consistent with this explanation. Regardless of the BMIz findings, a negative relationship existed between fat mass and FT4 in both the <10y and ≥10y groups. BMIz does not always accurately depict adiposity, particularly among African Americans (27), who made up a substantial part of this cohort. It is possible that more direct measures of fat mass than BMIz or extremely large sample sizes (25) are required to observe the BMI-FT4 relationship among young, growing children, since most of the pediatric studies that did not find this relationship used BMI in relation to FT4 status and had relatively smaller sample sizes (15–20, 22, 23). It is also possible that the greater amounts of fat mass found among obese adolescents exert greater physiological effects that are easier to observe.

At least some of the thyroid abnormalities observed in severe obesity are reversible with weight loss (28), suggesting the possibility of dysregulated signaling by obesity-related humoral factors. Potential causes of the observed thyroid dysregulation seen in obesity include adiposity-induced thyrotropin-releasing hormone (TRH) over-secretion, TSH resistance, or adaptations that increase energy expenditure (1, 26). Adipose tissue-derived leptin regulates energy balance in part through the hypothalamic-pituitary-thyroid axis by up-regulating hypothalamic TRH gene expression (1) and can also stimulate conversion of T4 to T3 via activation of thyroid deiodinases (1). Previous research supports the close relationship between thyroid hormones and leptin, in that a positive relationship has been found between TSH and leptin in longitudinal and cross-sectional analyses (19). Leptin has also been found to be inversely correlated with FT4 (12). In our analyses, we found a positive relationship between leptin and TSH in the DXA sample, but no associations between FT4 and leptin in either cohort.

Another possible cause for the observed thyroid dysregulation of obesity is thyroid hormone resistance. Adipocytes contain TSH receptors, and TSH may play a direct role in adipocyte differentiation, lipolysis, and adipokine production (29). In a study of 107 participants who were obese and 12 participants who were lean, subcutaneous and visceral adipose tissue mRNA expression of the TSH- and thyroid hormone receptors genes were decreased in individuals who were obese (5). Following weight loss, TSH, free triiodothyronine (FT3), and gene expression returned to normal levels (5).

Some have hypothesized that increased concentrations of TSH, driving greater T4 to T3 conversion in obesity, is a possible adaptive, counterregulatory mechanism that could increase metabolic rate and energy expenditure, thus preventing additional weight gain (26).

Indeed, in patients with accumulated central fat, the FT3:FT4 ratio is positively associated with waist circumference and BMI (3). This mechanism could be part of the difficulties often observed in humans attempting to maintain weight loss, because as weight falls, thyroid hormone concentrations and metabolic rate decrease (1, 26).

We also examined the relationship between thyroid status and lipid profiles. We found a positive relationship between TSH and TG and a negative relationship between FT4 and TG independent of body adiposity. Though data are mixed (4, 22), one prior study examining a pediatric sample of 1,210 participants also found the same relationships with TG, TSH and FT4, even when controlling for age, sex, and BMIz (24). The exact mechanism for this observation is unknown, though it is conceivable that the increased TSH of obesity influences the transport of TG in lipoproteins, reducing lipoprotein lipase activity and effectively increasing TG (30).

Ultimately, the question arises as to whether the observed thyroid dysregulation seen in patients with obesity is a consequence or cause of obesity, and whether it requires treatment (14). Most pediatric studies examining TH status in children who are obese have found that levels normalize following weight loss (15, 17–20, 22, 23, 31). However, some researchers believe that the thyroid dysregulation in children who are obese is a sign of subclinical hypothyroidism, which often leads to inflammation, insulin resistance, and dyslipidemia (26, 31). We believe that treatment of mild thyroid dysfunction with l-thyroxine in children who are obese is unnecessary, as TH concentrations normalize following weight loss and treatment with l-thyroxine in children who are obese does not improve blood lipids or factors related to weight status (26, 31). However, obesity does not protect against autoimmune thyroiditis, and this diagnosis should be entertained, evaluated, and treated in children with obesity with rising TSH (18, 19).

Strengths of this study include the large sample of children studied, the high percentage of participants who were severely obese, which improved the ability to detect obesity-associated changes in thyroid status, and the use, in addition to BMI, of DXA to examine associations between thyroid status and adiposity. Limitations include that we did not have FT3 available, and FT4 data were not available in some participants. Additionally, thyroid antibodies were not assessed in those with TSH <12 mIU/L; thus some patients with untreated or undiagnosed autoimmune thyroiditis may not have been excluded from analyses. The cross-sectional design also limits our understanding of the relationship between thyroid hormones and obesity. In particular, we could not delineate the potential effects of rapid growth during puberty on thyroid function tests.

In summary, we found that measures of adiposity were positively associated with TSH and negatively with FT4 in a large pediatric cohort. In the future, it would be worthwhile to examine these relationships in a large longitudinal sample to determine how TSH, FT3, and FT4 change over time in relation to weight and pubertal status, and also how these changes affect leptin and lipid concentrations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- In adults, high adiposity is associated with increased thyroid stimulating hormone (TSH) and decreased free thyroxine (FT4).
- Pediatric research into thyroid dysregulation and obesity is less consistent, likely due to varying ages, BMI-Z ranges, and sample sizes of cohorts.
- Some but not all studies find leptin is related to TSH and FT4 after controlling for measures of adiposity.

WHAT THIS STUDY ADDS

- In a large pediatric cohort (n=1203) oversampled for obesity, TSH was positively associated with both BMI-Z and fat mass.
- There was a negative correlation between FT4 and both BMI-Z and fat mass. However, the association between FT4 and adiposity was detectable only among children <10y only using fat mass, not BMI-Z, partially explaining observed inconsistencies in the pediatric literature.
- There was a significant positive relationship between leptin and TSH, even after controlling for fat mass, suggesting hyperleptinemia could contribute to TSH elevation.

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Table 1

Demographic, Anthropometric, and Laboratory Results of the BMI (A) and DXA (B) Cohorts

	A. BMI Cohort			B. DXA Cohort		
	Total N=1203	**Children with Obesity N=572**	**Children without Obesity N=631**	**Total N=829**	**Children with Obesity N=442**	**Children without Obesity N=387**
Sex, N (%)						
Female	787 (65.4)	374 (65.4)	413 (65.5)	576 (69.5)	308 (69.7)	268 (69.3)
Male	416 (34.6)	198 (34.6)	218 (34.5)	253 (30.5)	134 (30.3)	119 (30.7)
Race, N (%)						
Non-Hispanic Black	461 (38.3)	288 (50.3)	173 (27.4)	340 (41.0)	214 (48.4)	126 (32.6)
Non-Hispanic White	640 (53.2)	259 (45.3)	381 (60.4)	422 (50.9)	207 (46.8)	46 (11.9)
Other	102 (8.5)	25 (4.4)	77(12.2)	67 (8.1)	21 (4.8)	215 (55.5)
SES[#]	2.7±1.1 (1–5)	2.8±1.1 (1–5)	2.5±1.1 (1–5)	2.7±1.1 (1–5)	2.8±1.1 (1–5)	2.6±1.1 (1–5)
Puberty Stage[#]	2.2±.8 (1–3)	2.3±.8 (1–3)	2.0±.9 (1–3)	2.2±.8 (1–3)	2.4±.7 (1–3)	2.0±.9 (1–3)
Age (y)[#]	12.3±3.2 (5.0-18.0)	12.5±3.0 (5.5-17.9)	12.0±3.3 (5.0-18.0)	12.5±3.0 (5.0-21.1)	13.1±2.7 (6.4-21.1)	11.7±3.3 (5.0-20.5)
TSH (uIU/mL)[#]	2.1±1.1 (.1-8.8)	2.2±1.2 (.1-8.8)	1.9±1.0 (.3-7.2)	2.0±1.1 (.1-8.8)	2.0±1.1 (.1-8.8)	1.9±1.0 (.4-7.6)
Subclinical Hypothyroidism (%)[†]	3.1	4.8*	1.6	2.5	3.2	1.8
FT4 (ng/dL)[#]	1.24±.01 (.7-2.0)	1.20±.01 (.7-2.0)	1.29±.01 (.9-2.0)	1.2±.2 (.7-2.2)	1.2±.2 (.7-2.2)	1.3±.2 (.8-1.8)
Weight (kg)[#]	66.4±33.2 (15.6-199.9)	88.4±32.4 (21.9-199.9)	46.4±17.6 (15.6-89.2)	69.6±30.7 (15.0-171.1)	89.4±24.4 (32.0-171.1)	46.9±19.3 (15.0-90.3)
Height (cm)[#]	152.7±16.9 (101.0-197.1)	156.5±14.8 (101.0-191.5)	149.3±17.9 (107.3-197.1)	154.1±16.0 (108.3-192.5)	158.9±12.3 (121.9-190.4)	148.5±17.9 (108.3-192.5)
BMI (kg/m^2)[#]	27.1±10.3 (12.9-75.0)	35.1±9.4 (19.0-75.0)	19.9±3.8 (12.9-30.1)	28.0±9.5 (11.6-74.1)	34.9±7.2 (20.7-74.1)	20.2±4.3 (11.6-29.9)
BMIz[#]	1.4±1.2 (−2.3-3.4)	2.4±.4 (1.7-3.4)	.5±.8 (−2.3-1.6)	1.5±1.2 (−5.5-3.4)	2.3±.4 (1.7-3.4)	.5±.9 (−5.5-1.6)
Fat Mass (kg)[#]	–	–	–	26.6±17.2 (1.7-85.4)	38.7±13.4 (7.2-85.4)	12.7±8.2 (1.7-35.2)
Percent Fat[#]	–	–	–	34.5±11.2 (8.7-64.1)	42.5±6.0 (16.4-64.1)	25.3±8.4 (8.7-45.3)
Total Cholesterol (mg/dL)[#]	161.6±30.8 (72.0-291.0)	165.6±33.6 (72.0-288.0)	158.0±27.6 (84.0-291.0)	161.1±30.8 (67.0-319.0)	162.5±33.0 (67.0-319.0)	159.6±28.2 (94.0-280.0)
LDL-Cholesterol (mg/dL)[#]	95.6±27.7 (11.2-220.0)	101.0±30.0 (11.2-220.0)	90.7±24.4 (25.2-203.8)	95.0±27.6 (11.2-206.4)	97.7±29.1 (11.2-206.4)	91.9±25.5 (25.2-203.8)
HDL-Cholesterol (mg/dL)[#]	48.4±1.3 (22.0-117.0)	44.0±1.3 (22.0-81.0)	52.8±1.2 (26.0-117.0)	48.9±12.1 (22.0-117.0)	44.0±9.9 (22.0-83.0)	54.3±12.1 (26.0-117.0)

	A. BMI Cohort			B. DXA Cohort		
	Total N=1203	**Children with Obesity N=572**	**Children without Obesity N=631**	**Total N=829**	**Children with Obesity N=442**	**Children without Obesity N=387**
Triglycerides (mg/dL)[#]	70.5±1.7 (20.0-784.0)	85.3±1.7 (24.0-784.0)	59.3±1.6 (20.0-540.0)	74.4±1.7 (20.0-711.0)	90.9±1.7 (27.0-711.0)	59.3±1.6 (20.0-540.0)
Leptin (ng/mL)[#]	19.0±18.8 (.4-145.4)	31.6±19.5 (2.4-145.4)	7.9±8.3 (.4-51.9)	20.6±17.3 (.5-92.9)	31.2±16.2 (.9-92.9)	8.9±9.1 (.5-51.9)

[#]Mean±SD (Range).

[†]Subclinical hypothyroidism defined as TSH 4.5-10 uIU/mL

Table 2

ANCOVA for the BMI cohort with TSH (A) or FT4 (B) as the dependent variable

	A. TSH (uIU/mL) N=1192			B. FT4 (ng/dL) N=946		
	ß±SEM	**p**	**95% CIs**	**ß±SEM**	**p**	**95% CIs**
Sex						
Female	.028±.069	.681	−.107, .164	−.008±.006	.195	−.020, .004
Male	0[a]	–	–	0[a]	–	–
Race						
Non-Hispanic Black	−.210±.070	.003*	−.348, −.072	.007±.006	.249	−.005, .019
Other	−.022±.116	.853	−.250, .207	.012±.011	.295	−.010, .034
Non-Hispanic White	0[a]	–	–	0[a]	–	–
Puberty						
Prepubertal	.275±.143	.054	−.044, .555	.010±.013	.432	−.015, .035
Mid-Pubertal	.152±.102	.137	−.048, .352	−.013±.009	.154	−.032, .005
Late-Pubertal	0[a]	–	–	0[a]	–	–
BMIz	.157±.029	.000*	.101, .214	−.012±.003	.000*	−.017, −.007
Age (y)	−.013±.018	.481	−.048, .022	−.006±.002	.000*	−.009, −.003
SES	−.048±.030	.112	−.108, .011	−.008±.003	.001*	−.013, −.003

*Significant ß (p≤0.0125)

[a]Set to zero because redundant

Table 3

ANCOVA for DXA sample with TSH (A) or FT4 (B) as the dependent variable

	A. TSH (uIU/mL) N=819			B. FT4 (ng/dL) N=705		
	ß±SEM	**p**	**95% CIs**	**ß±SEM**	**p**	**95% CIs**
Sex						
Female	.156±.089	.080	−.019, .332	−.017±.017	.316	−.051, .017
Male	0[a]	–	–	0[a]	–	–
Race						
Non-Hispanic Black	−.222±.082	.007*	−.383, −.061	.004±.016	.805	−.028, .036
Other	.044±.142	.757	−.234, .322	.047±.031	.128	−.014, .107
Non-Hispanic White	0[a]	–	–	0[a]	–	–
Puberty Stage						
Prepubertal	.299±.173	.084	−.041, .639	.047±.034	.173	−.021, .115
Mid-Pubertal	.157±.118	.183	−.074, .389	.002±.024	.930	−.045, .049
Late-Pubertal	0[a]	–	–	0[a]	–	–
Fat Mass (kg)	.010±.003	.000*	.005, .015	−.002±.001	.000*	−.003, −.001
Age (y)	−.050±.026	.055	−.101, −.001	−.001±.005	.874	−.011, .010
SES	−.013±.036	.720	−.083, .057	−.013±.007	.075	−.027, .001
Height (m)	.425±.483	.379	−.523, 1.374	−.105±.097	.282	−.295, .086

*Significant ß (p≤0.0125)

[a]Set to zero because redundant

−Controlling for sex, race, puberty stage, age (y), SES, height (m), and fat mass (kg)