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Original Article

Triiodothyronine/Thyroxine Ratio and Metabolic Connections: Exploring Hyperthyrotropinemia in Childhood Obesity

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ABSTRACT

Objective: Subclinical hypothyroidism (ScH) is characterized by elevated thyroid-stimulating hormone (TSH) levels while serum thyroxine (T4) concentrations remain within normal limits. Despite the well-documented association between obesity and ScH, the underlying mechanisms remain poorly understood. This study aims to investigate thyroid functions in both obese and non-obese children and adolescents, examining TSH, T4, and T3 levels alongside anthropometric measurements and to explore potential associations between thyroid hormone levels and metabolic parameters in obese children.

Methods: In this retrospective study, medical records of children aged 5–18 years presenting for obesity evaluation were analyzed. Participants were categorized into two groups: Obese (body mass index [BMI] ≥95th percentile) and control (<95th percentile). The obese group was further stratified into those with high TSH (>4.5 μIU/mL) and normal TSH (≤4.5 μIU/mL). Anthropometric measurements, pubertal status, and biochemical parameters, including TSH, free triiodothyronine (fT3), fT4, and metabolic markers, were assessed.

Results: A total of 98 children (66 obese, 32 controls) were included. Within the obese group, children with high TSH exhibited significantly lower fT4 levels (p=0.021) but did not differ in fT3 levels, fT3/fT4 ratio, BMI, waist circumference, or metabolic parameters, including glucose, insulin resistance, and lipid profile. No significant correlation was observed between TSH levels and insulin resistance.

Conclusion: Our findings suggest that ScH in childhood obesity is associated with lower free thyroxine levels. However, metabolic alterations, including insulin resistance and dyslipidemia, were not found to be directly related to TSH levels. Future studies should aim to clarify the long-term implications of ScH in pediatric obesity and identify optimal management strategies for affected children.

INTRODUCTION

Subclinical hypothyroidism (ScH), also referred to as isolated hyperthyrotropinemia, is characterized by elevated thyroid-stimulating hormone (TSH) levels that exceed the upper limit of the reference range while serum thyroxine (T4) concentrations remain within normal limits.[1,2] Studies in children and adolescents estimate the prevalence of ScH to be between 1.7% and 2.9%.[1-4] Various factors contribute to its development, including Hashimoto's thyroiditis, iodine deficiency, mild congenital thyroid dysfunction due to genetic variants in the TSHR and DUOX2 genes, Down syndrome, certain medications, and obesity.[1]

The increasing prevalence of childhood obesity has emerged as a major public health issue, largely driven by excessive calorie intake and reduced physical activity. While genetic factors have also been implicated, pure endocrine disorders are rarely the primary cause of obesity.[5,6] Nevertheless, endocrine evaluations, including thyroid function tests, are routinely conducted in obese individuals. Mildly elevated TSH levels are commonly observed in this population, with ScH reported in 10–23% of obese children. Current evidence suggests that thyroid dysfunction is more likely a consequence rather than a cause of

weight gain, as studies have shown that TSH levels often normalize following weight loss interventions.[7-11]

Despite the well-documented association between obesity and ScH, the underlying mechanisms remain poorly understood. One hypothesis suggests that increased TSH levels may be an adaptive response to higher energy expenditure. Elevated free T3 and total T3 levels in obese individuals could enhance metabolic rate, thereby limiting excessive weight gain.[7-12] Another theory proposes a form of thyroid hormone resistance, as obesity has been associated with reduced T3 receptor expression and altered negative feedback mechanisms between TSH and peripheral thyroid hormones.[13] Additionally, neuroendocrine dysregulation may contribute to increased TSH secretion, while elevated leptin levels in obese individuals have been linked to enhanced hypothalamic TSH production.[12,13] Furthermore, inflammatory cytokines released by adipose tissue may impair thyroid hormone synthesis, potentially disrupting the normal feedback loop that regulates TSH secretion.

A useful indicator of thyroid hormone metabolism is the T3/T4 molar ratio, which reflects peripheral conversion of T4 to the metabolically active T3.[14] In obese individuals, this ratio is often elevated, suggesting increased deiodination of T4. While this may serve as a compensatory mechanism to enhance energy expenditure, its long-term impact on pediatric populations with ScH remains unclear.

This retrospective pilot study aims to investigate thyroid functions in both obese and non-obese children and adolescents, examining TSH, T4, and T3 levels alongside anthropometric measurements. Additionally, within the obese group, the study will explore potential associations between thyroid hormone levels and metabolic parameters.

MATERIALS AND METHODS

Study Design and Participants

This retrospective study analyzed patient records from October 1, 2021, to December 31, 2021. The study included children and adolescents aged 5-18 years who presented to the Pediatric Endocrinology Department (Dr. ME) for obesity evaluation. A control group of age- and sex-matched children without obesity was also included for comparison. Data on anthropometric measurements, pubertal staging (Tanner stage), and laboratory results were extracted from medical records and entered into a research database.

This study was observational, with no interventions performed, as all data were obtained retrospectively. Because the dataset was anonymized and no individual results were reported, the study was exempted from informed consent requirements. Ethical approval was granted by the Acıbadem Mehmet Ali Aydınlar University Ethics Committee (ATADEK 2019-17/17). All procedures adhered to the principles outlined in the Declaration of Helsinki.

Definition of Obesity and Study Groups

Obesity was defined as a body mass index (BMI) at or above the 95th percentile (corresponding to a BMI standard deviation score [SDS] of ≥1.64) for age and sex (6). Participants were categorized into two groups based on BMI: obesity (≥1.64 SDS) and control group (<1.64 SDS). Within the obesity group, patients were further stratified based on TSH levels, high TSH (>4.5 μIU/mL) and normal TSH (≤4.5 μIU/mL).[1]

Exclusion Criteria

Participants were excluded from the study if they met any of the following criteria

- Low fT4 or low fT3
- Autoimmune thyroid disease (positive anti-TPO and/or anti-TG antibodies, or sonographic evidence of thyroid parenchymal disorder)
- Risk of iodine deficiency (e.g., use of non-iodized salt)
- Use of medications known to affect thyroid function
- History of exposure to iodizing radiation
- Presence of chronic illnesses
- Incomplete laboratory data for thyroid functions

Data Collection

Anthropometric and clinical data recorded for all participants included, height, weight, and BMI SDS, Tanner stage (pubertal status) and systolic and diastolic blood pressure. In the obesity group, additional parameters were documented such as waist circumference (WC) and presence of acanthosis nigricans.

Anthropometric measurements were performed using a Harpenden stadiometer (Holtain) for height and a calibrated scale for weight. WC was measured at the midpoint between the lowest rib and the iliac crest. SDS were calculated using Turkish pediatric growth reference charts.[15,16]

Biochemical Analyses

Laboratory parameters included for both groups were free T3, free T4, and TSH and for the obesity group only were glucose, ALT, AST, and lipid profile.

Serum TSH, free T4 (fT4), free T3 (fT3), anti-TPO, anti-TG, and thyroid receptor antibodies (TRAb) were measured using an electrochemiluminescence immunoassay (ECLIA) on a Cobas e 801 analyzer (Roche Diagnostics, Australia). Thyroid-stimulating immunoglobulin (TSI) was assessed using the IMMULITE® 2000 TSI system (Siemens Healthcare Diagnostics, United Kingdom).

Blood samples were collected in the morning after an overnight fast. For the obesity group, additional metabolic parameters were measured, including fasting glucose, insulin, and lipid profile. Dyslipidemia was defined as Triglycerides >130 mg/dL, HDL cholesterol <40 mg/dL.[17]

Insulin resistance (IR) and secretion indices were assessed

using. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated by fasting glucose and insulin levels.

Statistical Analysis

Statistical analyses were conducted using SPSS version 16.0 (IBM Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean ± standard deviation (SD), median, frequency, percentage, minimum, and maximum values. The normality of data distribution was assessed using the Shapiro-Wilk test and graphical methods. For normally distributed variables, Student's t-test was used to compare two groups, while the Mann-Whitney U test was applied for non-normally distributed variables. Effect sizes as eta squared (η^2) and confidence intervals (95% CI) have now been included for key comparisons. Categorical variables were analyzed using the chi-square test or Fisher's exact test when appropriate. Correlations between variables were examined using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant.

For data visualization, 2D Kernel Density Estimation (KDE) was applied to smooth the distribution. The density of data points is represented using a color gradient, where lighter shades indicate higher concentrations. KDE ensures a continuous representation of data, reducing overplotting. The KDE approach smooths the distribution of data points to highlight regions of concentration (Fig. 1-3).

RESULTS

A total of 98 children (57 girls) aged between 5.0 and 17.6 years were included in the study. Participants were categorized based on BMI percentile into two groups: children with BMI >95th percentile (n=66) and children with BMI <95th percentile (n=32).

Anthropometric, clinical, and laboratory features of Obesity and Control groups were given in Table 1. Age, gender, and stages of puberty were similar between the two groups. Height SDS was significantly higher in the obesity group (1.1±1.5) compared to the controls (-0.1±1.5, p<0.001).

Acanthosis nigricans was significantly more prevalent in the obesity group (16.7%) than in the control group (0.0%, p=0.014).

TSH levels were significantly higher in children with BMI >95th percentile compared to those with BMI <95th percentile (p<0.001). However, no significant differences were found in fT3 (p=0.808), fT4 (p=0.246), or fT3/fT4 ratio (p=0.435) between groups.

A comparison of obese children with normal TSH and with high TSH is given in Table 2.

In the Obesity group, children with high TSH levels exhibited similar anthropometric indices, height, WC, and BMI SDS values compared to those with normal TSH (Table 2).

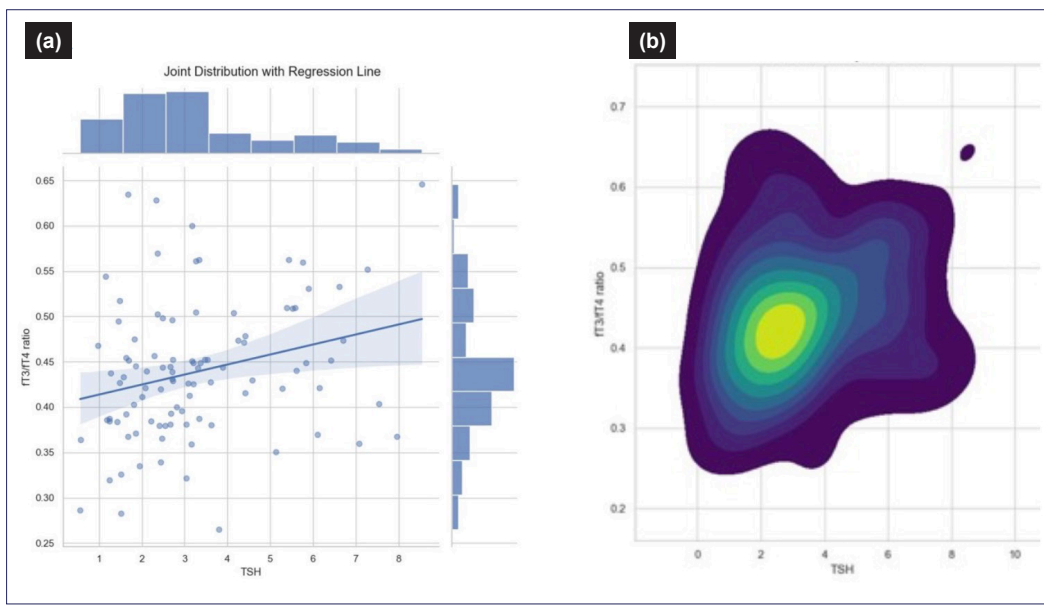

Figure 1. Relationship between fT3/fT4 (free triiodothyronine/ free thyroxine) ratio and TSH (thyroid stimulating hormone) levels. **(a)** Joint distribution plot with a regression line (Each point represents an individual from the dataset, with fT3/fT4 ratio on the x-axis and TSH levels on the y-axis. The regression line shows the overall trend, with a shaded confidence interval around it. The marginal histograms on the top and right display the distributions of fT3/fT4 ratio and TSH) **(b)** 2D Kernel Density Estimation (KDE) plot (The color intensity represents the density of data points, with brighter colors (yellow-green) indicating areas of higher density and darker colors (purple) showing lower density regions. The highest-density region (yellow-green) suggests that most individuals have TSH levels around 1–4 mU/L and fT3/fT4 ratios around 0.35–0.45. A smaller high-density cluster appears at a higher TSH level (~9 mU/L), possibly representing a distinct subgroup).

Table 1. Comparison of clinical and laboratory features between obese and control groups

	Obese (n=66)	Control (n=32)	p
Girls, n (%)	38 (57.6)	19 (59.4)	1.000
Age, years			
mean±SD (range)	11.4±3.1 (5.0-17.6)	11.0±3.2 (5.8-17.3)	0.596
Height SDS			
mean±SD (range)	1.1±1.5 (-2.3 – 3.9)	-0.1±1.5 (-2.8 – 3.7)	
median (IQR25-75)	1.2 (0.2 – 2.3)	-0.1 (-0.5 – 0.4)	<0.001
Body mass index SDS			
mean±SD (range)	2.8±0.8 (1.6 – 5.6)	-0.1±0.8 (-2.5 – 1.3)	
median (IQR25-75)	2.5 (2.3 – 3.0)	0.1 (-0.5 – 0.4)	<0.001
Pubertal, n (%)	46 (69.7)	20 (62.5)	0.498
Achantosis nigricans, n (%)	11 (16.7)	0 (0.0)	0.014
Waist circumference SDS			
mean±SD (range)	4.0±1.3 (-0.5-6.7)	N/A	
median (IQR25-75)	4.1 (3.3-4.9)		
Hypertension, n (%)	12 (18.2)	0 (0.0)	0.010
TSH µIU/mL			
mean±SD (range)	3.7±2.0 (0.6-8.6)	2.4±1.0 (1.0-4.4)	
median (IQR25-75)	3.2 (2.3-5.5)	2.4 (1.6-3.1)	<0.001
Free T3 pmol/L			
mean±SD (range)	6.8±1.0 (4.7-10.1)	6.8±1.0 (5.1-10.7)	
median (IQR25-75)	6.9 (6.1 – 7.4)	6.7 (6.2-7.2)	0.808
Free T4 pmol/L			
mean±SD (range)	15.5±2.2 (11.0-20.2)	16.1±2.1 (11.5-19.7)	
median (IQR25-75)	15.6 (13.8-17.2)	15.9 (14.1-17.6)	0.246
Free T3 / free T4 molar ratio	0.44±0.08	0.43±0.07	
mean±SD (range)	(0.26-0.65)	(0.32-0.63)	0.435
Glucose mg/dL			
mean±SD (range)	90.3±6.6	(74.0-110.0)	N/A
Hyperglycemia, n (%)	4 (6.1)	N/A	
Insulin µU/mL			
mean±SD (range)	22.1±15.1 (4.4-71.8)		
median (IQR25-75)	18.1 (10.1-31.0)	N/A	
HOMAIR			
mean±SD (range)	5.0±3.5 (0.9-15.6)		
median (IQR25-75)	3.9 (2.2 – 7.3)	N/A	
HbA1c %			
mean±SD (range)	5.5±0.3 (4.7-6.4)		
median (IQR25-75)	5.4 (5.3-5.6)	N/A	
Triglycerides			
mean±SD (range)	125.7±67.4 (44.0 – 386.0)		
median (IQR25-75)	113.5 (83.5-148.8)	N/A	
Hypertriglyceridemia, n (%)	13 (19.7)	N/A	
High-density lipoprotein cholesterol (HDL-C) mg/dL			
mean±SD (range)	45.8±9.9 (20.0 – 68.0)		
median (IQR25-75)	47.0 (38.0-51.0)	N/A	
Low HDL-C, n (%)	15 (22.7)	N/A	
Alanine aminotransaminase U/L			
mean±SD (range)	22.7±17.2 (8.0 – 124.0)		
median (IQR25-75)	17.5 (14.0-26.2)	N/A	
Aspartate aminotransaminase U/L			
mean±SD (range)	23.2±9.2 (8.0 – 66.0)		
median (IQR25-75)	23.0 (17.0 - 27.0)	N/A	

SDS: Standard deviation score; IQR: Interquartile range; Hb: Hemoglobin; HOMAIR: Homeostatic model assessment for insulin resistance; TSH: Thyroid-stimulating hormone.

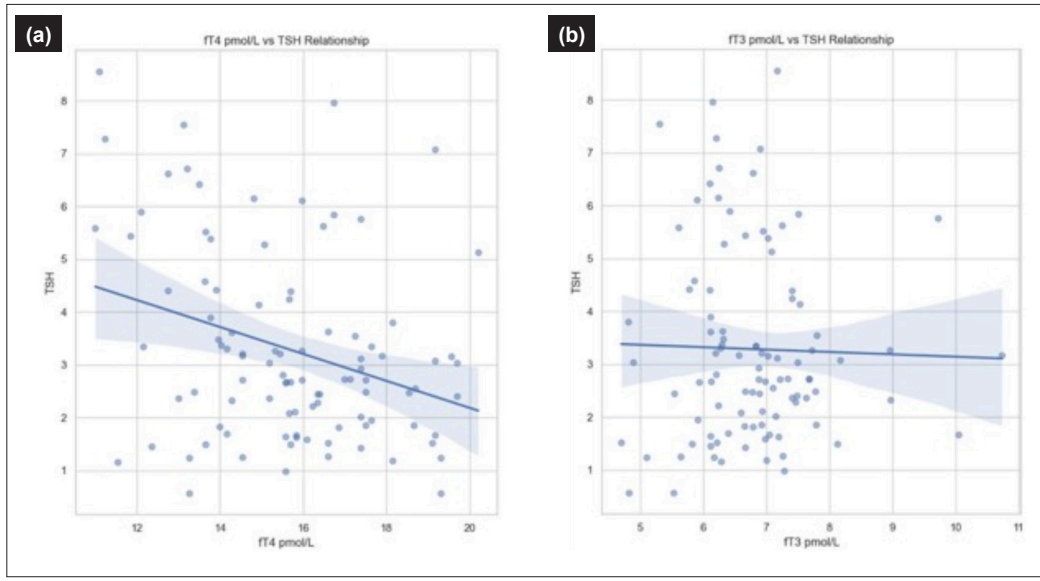

Figure 2. Relationship between thyroid hormones and TSH (thyroid stimulating hormone) (Scatter plots). **(a)** fT4 vs TSH. *There is a noticeable negative correlation, with higher TSH levels associated with lower fT4 levels, as indicated by the downward-sloping regression line and confidence interval indicates this inverse relationship*. **(b)** fT3 vs TSH. *There is a very weak or negligible correlation between TSH and fT3, as indicated by the near-horizontal regression line.*

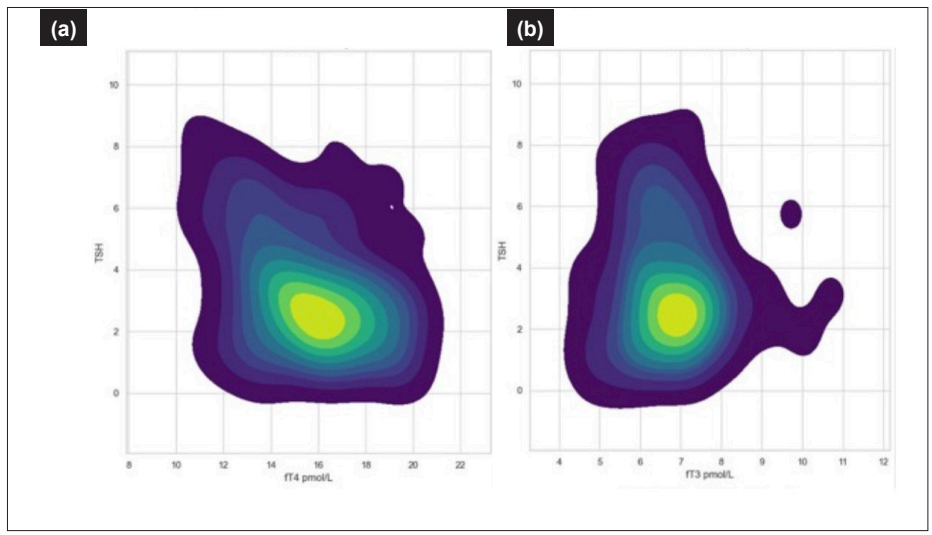

Figure 3. The distribution of TSH (thyroid stimulating hormone) levels against thyroid hormones (2D Kernel Density Estimation (KDE) plots). **(a)** TSH levels against fT4 (free triiodothyronine) levels . *The highest-density region (yellow-green) suggests that most individuals in the dataset have TSH levels around 1–4 mU/L and fT4 levels between 14–17 pmol/L. A broader spread in fT4 levels at lower TSH values is visible, while higher TSH values tend to associate with lower fT4 concentrations.* **(b)** TSH levels against fT3 (free triiodothyronine) levels. *The highest-density region (yellow-green) suggests that most individuals in the dataset have TSH levels around 1–4 mU/L and fT3 levels between 6–7 pmol/L. A smaller high-density cluster is visible at higher fT3 (~10 pmol/L) and TSH (~8 mU/L), potentially representing an outlier subgroup.*

While fT4 levels were lower in the high TSH group (14.4±2.6 pmol/L) compared to the normal TSH group (16.0±1.9 pmol/L, p=0.021), no significant differences were found in fT3 (p=0.477) or fT3/fT4 ratio (p=0.068). Other metabolic parameters, including glucose, insulin, HOMA-IR, and lipid profile, did not show significant differences between the normal and high TSH groups.

Correlation Analysis

Pearson correlation analysis was conducted to examine the relationships between fT3, fT4, fT3/fT4 molar ratio, TSH. The results revealed a significant positive correlation between fT3 and fT4 (r=0.283, p=0.005), as well as a strong positive correlation between fT3 and fT3/fT4 molar ratio (r=0.603, p<0.001). Additionally, fT4 was negative-

Table 2. Comparison of clinical and laboratory features among obese euthyroid children, obese children with subclinical hypothyroidism, and non-obese controls

	Obese		P			
	TSH normal (n=45)	TSH high (n=21)	95% CI (lower/upper) η^2	Control (n=32)	p*	p**
Girls, n (%)	25 (55.6)	13 (61.9)	0.627	19 (59.4)	0.739	0.854
Age, years	11.3±3.3	11.6±2.7	0.787	11.0±3.2	0.703	0.547
mean±SD (range)	(5.0-17.6)	(5.2-16.1)		(5.8-17.3)		
Height SDS	1.2	0.9	0.746	-0.1	0.001	0.010
median (IQR25-75)	(0.2 – 2.4)	(0.4 – 2.0)		(-0.5 – 0.4)		
Body mass index SDS	2.5	2.6	0.070	0.1		
median (IQR25-75)	(2.3 – 2.8)	(2.2 – 3.7)		(-0.5 – 0.4)	<0.001	<0.001
Pubertal, n (%)	29 (64.4)	17 (81.0)	0.252	20 (62.5)	0.861	0.222
Achantosis nigricans, n (%)	8 (17.8)	3 (14.3)	1.000	0.0 (0.0)	0.018	0.028
Waist circumference SDS	4.1	4.0	0.976	N/A		
median (IQR25-75)	(3.2-5.0)	(3.5-4.5)				
Hypertension, n (%)	10 (22.2)	2 (9.5)	0.311	0.0 (0.0)	0.004	0.152
TSH µIU/mL	2.5±0.9	6.2±1.0	<0.001	2.4±1.0		
mean±SD (range)	(0.6-4.4)	(4.6-8.6)	(-4.2/-3.2)	(1.0-4.4)	0.746	<0.001
			0.744			
Free T3 pmol/L	6.8±1.1	6.6±0.9	0.477	6.8±1.0	0.972	0.496
mean±SD (range)	(4.7-10.1)	(5.3-9.7)	(-0.35/0.74)	(5.1-10.7)		
			0.008			
Free T4 pmol/L	16.0±1.9	14.4±2.6	0.021	16.1±2.1	0.897	0.017
mean±SD (range)	(12.1-19.7)	(11.0-20.2)	(0.25/2.84)	(11.5-19.7)		
			0.166			
Free T3 / free T4 molar ratio	0.43±0.08	0.47±0.08	0.068	0.43±0.07		
mean±SD (range)	(0.26-0.63)	(0.35-0.65)	(-0.08/0.00)	(0.32-0.63)	0.969	0.065
			0.051			
Glucose mg/dL	90.4±6.4	90.1±7.5	0.865	N/A		
mean±SD (range)	(79.0-110.0)	(74.0-100.0)				
Hyperglycemia, n (%)	3 (6.7)	1 (4.8)	1.000	N/A		
Insulin µU/mL	17.8	18.2	0.961	N/A		
median (IQR25-75)	(9.3-31.0)	(12.8-32.4)				
HOMAIR	3.7	4.2	0.981	N/A		
median (IQR25-75)	(2.0 – 7.3)	(2.4 – 7.8)				
HbA1c %	5.5±0.3	5.4±0.3	0.795	N/A		
mean±SD (range)	(4.9-6.4)	(4.7-5.9)				
Triglycerides	128.5±72.4	115.1±45.4	0.564	N/A		
mean±SD (range)	(44.0 – 386.0)	(60.0 – 207.0)				
Hypertriglyceridemia, n (%)	10 (22.2)	3 (14.3)	1.000	N/A		
High-density lipoprotein cholesterol (HDL-C) mg/dL	45.4±10.1	47.3±9.4	.576	N/A		
mean±SD (range)	(20.0 – 67.0)	(33.0 – 68.0)	0			
Low HDL-C, n (%)	12 (26.7)	3 (14.3)	1.000	N/A		
Alanine aminotransaminase	23.0±18.4	21.5±11.5	0.811	N/A		
U/L, mean±SD (range)	(8.0 – 124.0)	(10.0 – 45.0)				
Aspartate aminotransaminase U/L, mean±SD (range)	22.7±9.6	25.6±6.7	0.403	N/A		
	(8.0 – 66.0)	(14.0 – 33.0)				

*obese euthyroid children vs non-obese controls. **obese children with subclinical hypothyroidism vs non-obese controls. SDS: Standard deviation score; IQR: Interquartile range; Hb: Hemoglobin; HOMAIR: Homeostatic model assessment for insulin resistance; TSH: Thyroid-stimulating hormon.

ly correlated with fT3/fT4 ratio (r= -0.578, p<0.001) and TSH (r= -0.312, p=0.002).

In the obesity group, no statistically significant correlations were observed between BMI SDS and thyroid function parameters.

Regarding metabolic parameters in the obesity group, fT3 demonstrated a significant positive correlation with AST (r=0.370, p=0.007), and fT4 demonstrated a significant negative correlation with HbA1c (r= -0.328, p=0.015). No statistically significant correlations were observed between HOMA-IR and lipid profile with thyroid function parameters.

Correlations between TSH, fT4, fT4 and fT3/fT4 ratio were given in Figure 1-3.

DISCUSSION

In this study, we explored the relationship between clinical, biochemical, and metabolic parameters in obese children with and without ScH. Contrary to our expectations, we did not observe a significant difference in the fT3/fT4 ratio, an indicator of peripheral thyroid hormone sensitivity, between obese children with elevated TSH and their euthyroid counterparts.

We initially hypothesized that obesity might alter thyroid hormone sensitivity, leading to increased TSH levels, and that the fT3/fT4 ratio could serve as a key marker for this effect. Corica et al.[14] similarly proposed that obesity may influence both central and peripheral thyroid hormone sensitivity, as well as metabolic markers. Their findings suggested that excess weight may affect tissue responsiveness to thyroid hormones, even in the presence of euthyroidism. However, the underlying mechanisms remain a topic of investigation, and further research is needed to determine whether these alterations represent a compensatory adaptation or an early marker of thyroid dysfunction.

There is a well-documented bidirectional relationship between the thyroid gland and adipose tissue. The adaptive changes within the hypothalamic-pituitary-thyroid (HPT) axis in response to the energy overload of obesity have been suggested to constitute a dynamic process aimed at maintaining homeostasis.[18] This balance may contribute to the increased cardiometabolic risk seen in obese individuals, as illustrated by the association between elevated TSH levels and obesity-related inflammation.[19] Some studies have proposed that altered thyroid hormone sensitivity—both centrally and peripherally—could be an early consequence of this imbalance, even in the absence of overt hypothyroidism. However, whether these changes are causal, compensatory, or secondary to metabolic disturbances remains unclear.

Although we did not find a significant association between HOMA-IR and thyroid hormones, Corica et al.[14] reported that an increased fT3/fT4 ratio was significantly influenced by the presence of insulin resistance. They acknowledged the limitations of their study, including a small, homogeneous population and the lack of literature to support their findings. The role of thyroid hormone sensitivity in obesity remains uncertain, with conflicting findings in the existing literature. Some studies suggest an association between increased central thyroid hormone resistance and metabolic conditions such as obesity and diabetes, whereas others report that decreased central sensitivity to thyroid hormones may be linked to a lower risk of prediabetes.[20,21]

Thyroid hormones are essential regulators of metabolism. While T3 is also directly secreted by the thyroid gland, it is primarily produced through the peripheral conversion of T4 by iodothyronine deiodinase (DIO) enzymes. Genetic variations affecting DIO enzyme activity may contribute to individual differences in T3 levels. In obesity, potential alterations in DIO activity have been hypothesized to disrupt the balance between T4 and T3, thereby influencing TSH regulation through negative feedback mechanisms.[22]

Interestingly, this contrasts with findings in hypothyroid individuals receiving long-term levothyroxine (L-thyroxine) therapy, where an unphysiological T4/T3 ratio is often observed, with disproportionately high T4 levels compared to healthy individuals.[22-24] Exogenous thyroxine treatment suppresses deiodinase 2 (D2) activity in peripheral tissues, impairing local T3 production while preserving hypothalamic and pituitary D2 function.[22,25] This discrepancy allows for normalization of serum TSH while peripheral tissues remain relatively T3-deficient, potentially leading to persistent hypothyroid symptoms.[26,27] However, our findings suggest that in obesity, the T3/T4 ratio does not exhibit a clear relationship with TSH levels, suggesting that thyroid hormone metabolism in obesity follows a different regulatory mechanism than in LT4-treated hypothyroid patients.

Another important finding in our study was that obese children with ScH did not exhibit significant differences in metabolic parameters compared to euthyroid obese children. In contrast, Carreras-Badosa et al.[28] reported that higher fT3 levels were associated with increased BMI, systolic blood pressure, and insulin resistance in euthyroid children with elevated TSH, suggesting that subtle thyroid dysfunction may contribute to metabolic disturbances over time. Similarly, Tersander et al.[29] found that ScH in obese children was linked to higher triglyceride levels but did not significantly affect basal metabolic rate, suggesting that ScH may have selective metabolic effects. Other studies have proposed that ScH in pediatric obesity could be associated with impaired glucose metabolism. Corica et al.[14] suggested that prepubertal children with obesity may exhibit alterations in central and peripheral thyroid hormone sensitivity, which could correlate with the severity of obesity and insulin resistance.

Notably, we found that fT4 levels were significantly lower in obese children with ScH. This finding is consistent with results from a Mendelian randomization study that explored the potential causal relationship between obesity and hypothyroidism.[30] That study also reported sig-

nificant differences in T4, fT4, and TSH levels between obese individuals with and without ScH, identifying fT4 as an independent risk factor for obesity complicated by ScH, even in the absence of significant differences in BMI or lipid profiles between the groups. However, this association was observed even in the absence of significant differences in BMI or lipid profiles between the groups, indicating that additional factors may contribute to this relationship.

Our study has several limitations that should be considered. The relatively small sample size and the cross-sectional study design limit our ability to draw causal conclusions regarding the relationship between ScH and metabolic dysfunction.

Conclusion

In conclusion, our findings suggest that subclinical hypothyroidism in childhood obesity is associated with lower free thyroxine levels. However, metabolic alterations, including insulin resistance and dyslipidemia, were not found to be directly related to TSH levels. Future studies should aim to clarify the long-term implications of subclinical hypothyroidism in pediatric obesity and identify optimal management strategies for affected children.

Ethics Committee Approval

The study was approved by the Acıbadem Mehmet Ali Aydinlar University Ethics Committee (Date: 28.01.2022, Decision No: ATADEK 2019-17/17).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.E., S.A.; Design: S.A.; Supervision: S.A.; Materials: E.K.O., M.E.; Data Collection and/or Processing: E.K.O., M.E.; Analysis: S.A., M.E.; Literature search: S.A., M.E.; Writing: S.A., M.E.; Critical revision: S.A., M.E.

Conflict of Interest

None declared.

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Triiyodotironin/Tiroksin Oranı ve Metabolik Bağlantılar: Çocukluk Çağı Obezitesinde Hipertirotropineminin Araştırılması

Amaç: Subklinik hipotiroidizm (SH), serum tiroksin (T4) konsantrasyonları normal sınırlarda iken yüksek tiroit uyarıcı hormon (TSH) seviyeleri ile kendini gösterir. Obezite ve SH arasındaki iyi bilinen ilişkiye rağmen, altta yatan mekanizmalar tam olarak anlaşılamamıştır. Bu çalışmanın amacı hem obez hem de obez olmayan çocuk ve ergenlerde tiroit fonksiyonlarını araştırmak, antropometrik ölçümlerin yanı sıra TSH, T4 ve T3 düzeylerini incelemek ve obez çocuklarda tiroid hormon düzeyleri ile metabolik parametreler arasındaki potansiyel ilişkileri araştırmaktır.

Gereç ve Yöntem: Bu retrospektif çalışmada, obezite değerlendirmesi için başvuran 5-18 yaş arası çocukların tıbbi kayıtları analiz edilmiştir. Katılımcılar iki gruba ayrılmıştır: Obez (vücut kitle indeksi [VKİ] ≥95. persentil) ve kontrol (<95. persentil). Obez grup ayrıca yüksek TSH (>4,5 µlU/mL) ve normal TSH (≤4,5 µlU/mL) olarak iki ayrı grupta incelenmiştir. Antropometrik ölçümler, pubertal durum ve TSH, serbest triiyodotironin (fT3), fT4 ve metabolik belirteçler dahil olmak üzere biyokimyasal parametreler değerlendirilmiştir.

Bulgular: Toplam 98 çocuk (66 obez, 32 kontrol) çalışmaya dahil edildi. Obez grupta, yüksek TSH'lı çocuklar anlamlı derecede düşük fT4 seviyeleri sergilemiş (p=0.021) ancak fT3 seviyeleri, fT3/fT4 oranı, BMI, bel çevresi veya glukoz, insülin direnci ve lipid profili gibi metabolik parametreler açısından farklılık göstermemiştir. TSH düzeyleri ile insülin direnci arasında anlamlı bir korelasyon gözlenmemiştir.

Sonuç: Bulgularımız çocukluk çağı obezitesinde subklinik hipotiroidizmin düşük serbest tiroksin düzeyleri ile ilişkili olduğunu göstermektedir. Bununla birlikte, insülin direnci ve dislipidemi gibi metabolik değişiklikler TSH düzeyleri ile doğrudan ilişkili bulunmamıştır. Gelecekteki çalışmalar, pediatrik obezitede subklinik hipotiroidizmin uzun vadeli etkilerini netleştirmeyi ve etkilenen çocuklar için en uygun yönetim stratejilerini belirlemeyi amaçlamalıdır.

Anahtar Sözcükler: fT3/fT4 oranı; obezite; subklinik hipotiroidizm; TSH.