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Original article

Is Waist-Height Ratio Associated with Thyroid Antibody Levels in Children with Obesity?

Ozcabi B et al. Thyroid Antibodies and Central Adiposity

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What is already known on this topic?
It is known that obesity influences thyroid functions. It has been recently reported that thyrotropin levels were associated with body mass index standard score deviation and waist-height ratio (WHtR) – an indicator of central fat accumulation- in obese children. In adults with obesity, it has also been revealed that thyroid autoantibody levels were higher than healthy subjects. However, in children with obesity, thyroid autoimmunity is not considered to be as evident as in adults considering that it has been previously reported that autoimmune thyroiditis was detected in only 19.5% of obese children with hyperthyrotropinemia.

What this study adds?
Although a correlation between WHtR and thyrotropin-thyroxine levels was detected, its association with thyroid autoantibody levels still remains unclear in obese children. This study is aimed to investigate whether there is an association between central fat accumulation and autoimmunity in children with obesity.

Abstract
Objective: Obesity is known to affect thyroid functions. Recently, waist-height ratio (WHtR) has been considered as a useful marker of subclinical hypothyroidism in obese cases, but its relation with thyroid autoimmunity still remains unclear. We evaluated the effect of body fat mass, WHtR, and metabolic parameters on thyroid autoantibody levels in children with obesity.
Methods: This is a cross-sectional study carried out with an obese (n=56, M/F:29/26) and a healthy group (n=38, M/F:19/19). All subjects underwent anthropometric measurements, laboratory investigations for thyroid function tests, thyroid peroxidase (TPO-ab) and thyroglobulin antibodies (Tg-ab), transaminase, blood glucose, insulin levels, and lipids after overnight fasting. Fat mass was estimated by multiple frequency bioimpedance analysis in the obese group, which was further divided into two subgroups according to the median of WHtR. All parameters were compared between the groups/subgroups.
Results: In the obese group, weight, height, body mass index (BMI), free-triiodothyronine, thyrotropin, TPO-ab, insulin, LDL-cholesterol, total cholesterol, alanine aminotransferase levels, and HOMA-IR were significantly higher than the controls group ($p<0.05$ for all). Median of WHtR was 0.6 in the obese group. In the "WHtR >0.6" subgroup (n=28), weight, BMI, fat mass, TPO-ab, Tg-ab, insulin and triglyceride levels were higher than WHtR ≤0.6 subgroup ($p<0.05$). A positive correlation was obtained between Tg-ab and WHtR (rho=0.28, p=0.041).
Conclusions: Euthyroid children with obesity and a WHtR >0.6 are likely to have higher thyroid antibody levels, and Tg-ab levels have a positive correlation with WHtR, which reveals an association of central adiposity with thyroid autoantibody levels in these cases.
Keywords: Free thyroxine, Free triiyodotironin, Thyroglobulin antibody, Thyroid peroxidase antibody, Thyroid stimulating hormone, Waist-height ratio

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Introduction

Obesity leads to a number of metabolic and hormonal disturbances in children, such as thyroid dysfunction (1,2). Moderate elevation of thyrotropin (TSH) levels (subclinical hypothyroidism) is a common condition in children with overweight/obesity, with a prevalence ranging from 7 to 23%. However, prior studies offer conflicting results about thyroid hormone levels (2-12). Nonetheless, it is accepted that TSH and thyroid hormone levels usually normalize with weight loss, from which it was interpreted that this is an adaptive response to lipid accumulation (2-4).

Anthropometric measurements are mostly used to diagnose and evaluate obesity and its complications (1). So far, a positive correlation between body mass index (BMI) and TSH has been revealed in numerous studies, and some follow-up studies have demonstrated that TSH level increases with weight gain and decreases with weight loss (2-9). Besides, some other anthropometric measurements have also been evaluated in several studies (1,4-6,8,9). In a study with a large cohort, TSH levels were reported to be associated positively with BMI standard deviation score (SDS) and waist/height ratio (WHtR), regardless of age, gender and pubertal stage. However, serum free thyroxine (fT4) concentrations were found to be associated with only WHtR (5). In another study, waist/hip ratio was considered as a predictor of increased free triiodothyronine (fT3) to fT4 ratio (9). These results suggest that central obesity could increase the risk of concurrent thyroid abnormalities in children with obesity (5,9).

Although TSH and thyroid hormone levels in children and adults with obesity have been evaluated in numerous studies, the effect of obesity and lipid accumulation on thyroid autoantibody levels still remains unclear in children (2-12). Obesity is well known to be a chronic inflammatory process (1). Elevated thyroid autoantibody levels (especially antithyroid peroxidase) with hypothyroidism have been reported to be common in adults with obesity (10). In addition, increased leptin levels have been found to be associated with the presence of autoimmune thyroiditis (AITD) (10). However, results of the studies about childhood obesity are slightly different, and non-autoimmune thyroiditis should be considered in the differential diagnosis before diagnosing AITD (3,12,13). It was observed that obese cases with hyperthyrotropinemia and hypoechogenicity in thyroid ultrasound without antibody seropositivity had normal cytological findings in biopsy specimens, which indicates the important role of thyroid antibodies in a diagnosis of AITD in obese patients (13). Autoimmune thyroiditis was detected in only 19.5% of children with obesity and hyperthyrotropinemia and 7.4% in children with normal TSH levels (3, 12). Moreover, it has been shown that antithyroid peroxidase antibody (TPO-ab) level was positively associated with BMI (7).

Obesity and central fat accumulation lead to insulin resistance and dyslipidemia (1). In previous studies, TSH levels were found to correlate with fasting insulin (6), total cholesterol (6,11), triglyceride levels (6,8,11,14) and HOMA-IR (6). However, little is known about the association of thyroid antibody levels and metabolic disturbances in children with obesity.

The aim of this study is to evaluate the association of thyroid hormone and autoantibody levels with body fat mass, WHtR and metabolic parameters, such as lipid profile, fasting glucose and insulin levels in euthyroid children with obesity.

Patients and Methods

Study population

In this cross-sectional study, 55 obese and 38 healthy children aged between 8 and 18 years were involved. The obese group was consisted of subjects without additional endocrine/genetic disorders leading to obesity. The control group was consisted of age- and sex-matched children who admitted to the pediatric clinic for routine health screening. Cases who were previously diagnosed with overt or subclinical hypothyroidism, AITD, who had a family member with a diagnosis of AITD or who were receiving medication affecting energy metabolism, such as metformin were excluded from the study.

Anthropometric measurements and puberty stage:

All the measurements were obtained by the same clinician at admission. Height was measured using a stadiometer (Holtain Limited, Crymych, Wales) to the nearest 0.5 cm with the subject naked feet, eyes looking straight ahead, back against the wall. Weight was measured using an electronic scale (Tefal, France) sensitive to 100 g and BMI was calculated as weight in kilograms divided by the square of height in meters. The waist circumference (WC) was measured in obese group midway between the lowest rib and the superior border of iliac crest at the end of normal expiration, at a parallel level to the floor with a non-stretchable tape to the nearest 0.1 cm. The SDS and percentiles were calculated according to Turkish children reference values previously reported by ÇEDD Çözüm/TPEDS Metrics (15,16). The patients with BMI percentile ≥95 for sex and age were defined as obese (1). Puberty stage was defined according to Tanner Marshall staging (17).

Assessment of body composition:

Body composition including fat mass (kg) was estimated by multiple frequency bioimpedance analysis (BIA) in the obese group. Measurements were performed by the same physician using a portable body bioimpedance spectroscopy device [the Body Composition Monitor (BCM), Fresenius Medical Care, Germany]. Fat mass index (FMI) was calculated as the quotient of fat mass/height^2. Fat mass to weight ratio (fat%) was described as the quotient of fat mass/body weight x 100. All anthropometric measurements and body composition analyses were carried out at the same study visit and obtained after overnight fasting.

Blood sample collection:

Serum specimens collected from the patient and healthy control groups were stored at -80 °C until the ELISA tests were performed. Routine biochemical tests were analyzed in Cental Biochemistry Laboratory, Cerrahpasa Faculty of Medicine. Fasting blood glucose, total cholesterol, HDL-C, LDL-C and triglyceride levels were measured by enzymatic, colorimetric methods, aspartate amino transferase (AST) and alanine aminotransferase (ALT) by kinetic UV methods in Roche Modular System. Insulin level was measured by solid phase sandwich ELISA (DRG instruments GmbH, Germany). Insulin resistance was assessed using the homeostasis model assessment for insulin resistance (HOMA-IR), which was calculated using the following formula: glucose (mg/dL) x insulin (μIU/mL) / 22.5 (18).

Thyroid function and autoantibody tests:

For the quantitative analysis of fT3 (free triiodothyronine, DRG Instruments GmbH, Germany, Catalog No: EIA-2385) (intra-assay CV: 3.6 %, inter-assay CV:7.9 %), fT4 (free thyroxine, DRG Instruments GmbH, Germany, Catalog No: EIA-2386) (intra-assay CV: 4.26%; inter-assay CV: 6.01%), and TSH (TSH, DRG Instruments GmbH, Germany, Katalog No: EIA-4171) (intra-assay CV: 5.7%; inter-assay CV: 7.1%) commercial EIA (Enzyme Immunoassay) kits were used, according to the manufacturer's guidelines.
A TSH level <5 μU/mL was defined as 'normal'; and, reference intervals for ft4 and ft3 levels were 0.7-1.6 ng/dL and 1.71-3.72 pg/mL respectively. The patients were considered to be euthyroid if their serum fT4 and TSH levels were within normal range (19). The TPO-ab and Tg-ab levels were measured by chemiluminescence method using the Roche Modular System (Germany). A TPO-ab level >34 IU/mL and a Tg-ab level >115 IU/mL were described as 'positive'.

Statistical analysis:

All data were controlled for normal distribution. Normally distributed data were presented as mean ±SD, and nonparametric data were presented as median (interquartile range). Between group comparisons Fischer's exact test or Mann-Whitney U test according to a normal or a nonparametric distribution of the tested variable. Pearson's correlation investigated the relation between normally distributed quantitative data, while Spearman's rank correlation was used otherwise. Obese cases were divided into two different groups according to the median value of WHtR. The association between thyroid antibodies and WHtR were tested with univariate analysis in the obese group. Biostatistical analysis of the study results was performed by SPSS (Statistical Package for Social Sciences) software, Version 21.0 (SPSS Inc., Chicago, IL, USA) and p values <0.05 were considered statistically significant.

Informed consent and ethics committee approval:

The study was approved by the Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine Ethical Committee (date: 04.02.2020: ethics approval number: 21299). Patients were included in the study following a consent form signed by parents/caregivers. The information about the patients was kept confidential and used only for the purposes of the study.

Results:

The study subjects consisted of the obese (n=55, M/F:29/26) and healthy groups (n=38, M/F:19/19) with a mean age of 12.4±2.6 years. The 78.5% (n=73) of the patients were pubertal. Between the two groups, age, gender and pubertal stages were indifferent (p>0.05). Serum TSH, fT4, fT3 and thyroid autoantibody levels of all subjects were within normal ranges. Weight and weight SDS, BMI and BMI SDS were higher in the obese group compared to controls. In laboratory findings, fasting insulin, ALT, fT3, TSH, TPO-ab levels and HOMA-IR were higher, fT4 was lower in children with obesity than the healthy control (p<0.001). Anthropometric measurements, metabolic parameters, thyroid function test and autoantibody levels are summarized in Table 1.
The mean value of the WC, WHtR, fat% and fat mass index (FMI) of obese patients were 97.3±13.6, 0.61±0.06, 39.2±5.7 and 16.6±4.2, respectively.
In children with obesity, WHtR was significantly correlated with Tg-ab (p=0.041, r=0.28), triglyceride level (p=0.011, r=0.35), fat% (p<0.001, r=0.52) and FMI (p<0.001, r=0.62) (Figure 1).
Although the cut-off value of WHtR for predicting subclinical hypothyroidism has previously been proposed as 0.5 (5), in our cohort, we couldn't find any significant difference in thyroid antibody levels between the patients with a WHtR above and below 0.5 (p>0.05). As no other cut-off value has been reported to predict an increase in thyroid antibody levels, we further divided obese cases into two different groups according to the median WHtR, which is 0.6: patients with a WHtR ≤0.6 and patients with a WHtR >0.6. As expected, in the WHtR >0.6 group, weight, BMI and their SDSs were significantly higher as well as fat% and FMI than the WHtR ≤0.6 group. Although no significant difference was obtained for TSH and thyroid hormone levels, both thyroid autoantibody levels were significantly higher in the WHtR >0.6 group. Among the metabolic parameters, triglyceride and fasting insulin levels were significantly higher in the WHtR >0.6 group (p<0.05) (Table 2). Anthropometric measurements, metabolic parameters, thyroid function test and autoantibody levels of the two subgroups are summarized in Table 2.
Univariate analysis revealed a significant difference in TPO-ab and Tg-ab levels between WHtR ≤0.6 and WHtR >0.6 subgroups with an odd ratio (OR) of 0.262 and 0.275 respectively (Table 2).

Discussion:

This study revealed an association between WHtR and thyroid antibody levels, particularly Tg-ab. Thyroid antibody levels were higher in patients with obesity, as well as WHtR, BMI and BMI SDS, fat mass, fasting insulin and triglyceride levels which may suggest that lipid accumulation and particularly central obesity influence the thyroid antibody production.

In our study, fT3 and TSH levels were significantly higher and fT4 levels were significantly lower in euthyroid children with obesity compared to controls. Although there are some studies with diverse outcomes, our results are similar to those of Marwaha et al (7), who have shown higher TSH and fT3 levels and lower fT4 levels in obese euthyroid children. Leptin effect, enhanced deiodination of thyroid hormones, blunted feed-back response of TSH release to circulating fT3, promoting action of TSH on adiposity and insulin resistance have all been considered as the probable causes of this condition (7).

Anthropometric measurements, such as BMI SDS and WHtR have been recently associated with TSH and thyroid hormones (4-6,8). Dahl et al. (5) reported that TSH concentrations were associated positively with WHtR, and they concluded that the OR of exhibiting subclinical hypothyroidism was 1.8 when presenting with a WHtR >0.5. However, no cut off value of WHtR was reported to predict an increase in thyroid autoantibody levels. Our study revealed that children with obesity and a WHtR >0.6 (the median value of the obese group) had significantly higher TPO-ab and Tg-ab levels even in the absence of hyperthyrotropinemia with an OR of 0.262 and 0.275 respectively, and in these patients BMI, BMI SDS, fat% and FMI were significantly higher. The anthropometric and biometric measurements such as BMI, BMI SDS, fat%, FMI and WHtR have been associated with lipid accumulation, adipocytokines, such as leptin and some other inflammatory markers (1). It has previously been shown that leptin had a role to regulate the T helper-1 response and the proliferation of CD4+ and CD25+ cell clone involving in the apoptotic process leading to AITD (20,21). In adults, leptin concentration has also been associated with AITD regardless of bioanthropometric variables (10). In this study, we have additionally observed a weak but significant, positive correlation between WHtR and Tg-ab level, but no significant correlation was obtained between BMI and Tg-ab levels in children with obesity. Thus, we suggest that abdominal obesity may be a better predictor of thyroid autoimmunity than BMI in obese cases, which only reflects the obesity degree rather than its distribution.

Our results indicate that the levels of thyroid antibodies seem to increase despite the absence of thyroid dysfunction, hyperthyrotropinemia and autoantibody seropositivity in children with obesity. Also, in children with obesity and a WHtR >0.6, thyroid antibody levels -particularly Tg-ab- were higher and only Tg-ab levels have been found to be associated with central fat accumulation contrary to TPO-ab levels. Despite that TPO-ab positivity has been reported to be a common condition in healthy population with a prevalence of 12-26%, the prevalence of Tg-ab positivity was found to be similar to TPO-ab positivity in adults with obesity (15% versus 14%), which also supports that Tg-ab levels are somewhat more related to obesity than TPO-ab levels, which raises the question: "Can obesity elevate a specific type of thyroid autoantibody?", but more data is needed to clarify this point (22,23). On the other hand, as the increase in thyroid autoantibodies may result from both AITD and obesity, "Does this finding complicate the diagnosis and management of AITD in children with obesity?", in other words, "Does the increase in antibody levels suggest AITD or is it just the result of obesity?". We consider that it is unnecessary to investigate the thyroid antibody levels routinely in children with obesity, especially when the thyroid function tests are within normal limits. In cases of seropositivity, a certain distinction of AITD may be challenging, given that thyroid changes in ultrasound is a common finding in cases with obesity (12). Further long-term follow-up studies investigating if weight loss reverses the abnormal findings in ultrasound and leads to a decrease in levels of thyroid autoantibodies would shed light this topic.

As expected, fasting insulin and triglyceride levels were significantly higher in the WHtR >0.6 subgroup compared to the WHtR ≤0.6 subgroup as high WHtR is associated with high fat mass and central lipid accumulation (1,9). The relation between thyroid function tests and lipid profile in obese subjects shows variations in different studies. Unuvar et al. (8) have previously reported that triglyceride level was the strongest independent variable correlated with TSH level in children with obesity. Shalitin et al. (14) found a positive correlation between TSH and triglyceride levels, whereas Reinehr at al. (24) could not find any correlation between TSH and lipid profile in their study conducted with 246 children with obesity.

Despite a large number of studies on thyroid hormones and TSH in childhood obesity, there is few data about the association between thyroid autoantibody levels and metabolic parameters of obesity, such as insulin/glucose levels, HOMA-IR, and lipid profile. We did not find any correlation between these parameters and thyroid antibody levels. It has recently been shown that TPO-ab and Tg-ab levels were not significantly different in obese children with and without insulin resistance (9). In adults with obesity, no association was found between thyroid antibody positivity, insulin resistance and atherogenic dyslipidemia (23). However, Tamer et al. (25) revealed that TPO-ab levels were positively correlated with triglyceride levels and WC, and negatively correlated with HDL-C levels in premenopausal women with Hashimoto thyroiditis, whereas Tg-ab was correlated with triglyceride and non-HDL-C levels (24). In these patients, no correlation was found between TSH levels and lipid profile. The investigators suggested that thyroid autoimmunity could be associated with hyperlipidemia, independent of thyroid function. The association between thyroid antibody levels and insulin resistance and/or lipid profile still remains unclear and further investigations in adults and children are needed.

Study limitations and strengths

Ultrasound imaging of thyroid gland was not performed. However, this is a minor setback because thyroid changes on ultrasound may also be due to non-autoimmune thyroiditis, which is an important entity on this topic (12). Due to limited number of study group and study design, we could not obtain a cut-off value of WHtR to predict the presence of thyroid autoimmunity. Nevertheless, univariate analysis showed a significant difference in TPO-ab and Tg-ab levels when we divided the obese subjects into two subgroups according to the median WHtR value "0.6" in our study. Iodine levels were not studied which can also be effective in thyroid autoimmunity. Mediators such as leptin, adiponectin and resistin which may have a link between autoimmunity and fat accumulation were not studied.

The strength of the study is that the impact of lipid accumulation (estimated by bioelectrical impedance analysis) and central adiposity (described as WHtR) on thyroid function and autoantibodies were both evaluated, and their association with metabolic parameters were all presented.

Conclusion:
This study revealed that euthyroid children with obesity had higher thyroid autoantibodies compared to the controls and the obese patients with a WHtR >0.6 had higher thyroid antibody levels compared to those with WHtR ≤0.6 even in the absence of AITD, and there was a positive correlation between WHtR and Tg-ab levels. These findings suggest that central adiposity influences thyroid autoantibody production in children with obesity. Further studies with larger number of participants are needed to determine the effect of central adiposity and its alterations on the thyroid autoimmunity and efficacy of WHtR in clinical practice on this issue.

Ethics

Ethics Committee Approval: The study was approved by the Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine Ethical Committee (date: 04.02.2020: ethics approval number: 21299).

Informed Consent: Patients were included in the study following a consent form signed by parents/caregivers. The information about the patients was kept confidential and used only for the purposes of the study.

Authorship Contributions

Surgical and Medical Practices: Bahar Özcabı, Gürkan Tarçın, Esma Şengenç, Feride Tahmiscioğlu Bucak,
Concept: Olcay Evliyaoğlu, Bahar Özcabı
Design: Olcay Evliyaoğlu, Bahar Özcabı
Data Collection or Processing: Bahar Özcabı, Gürkan Tarçın, Esma Şengenç, Feride Tahmiscioğlu Bucak
Analysis or Interpretation: Bahar Özcabı, Olcay Evliyaoğlu
Literature Search: Bahar Özcabı, Gürkan Tarçın, Esma Şengenç, Feride Tahmiscioğlu Bucak, Olcay Evliyaoğlu
Writing: Bahar Özcabı, Gürkan Tarçın, Esma Şengenç, Feride Tahmiscioğlu Bucak, Oya Ercan, Ibrahim Murat Bolayırlı, Olcay Evliyaoğlu

Conflict of Interest: No conflict of interest

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Figure 1. Is waist-height ratio associated with thyroid antibody levels in obese children

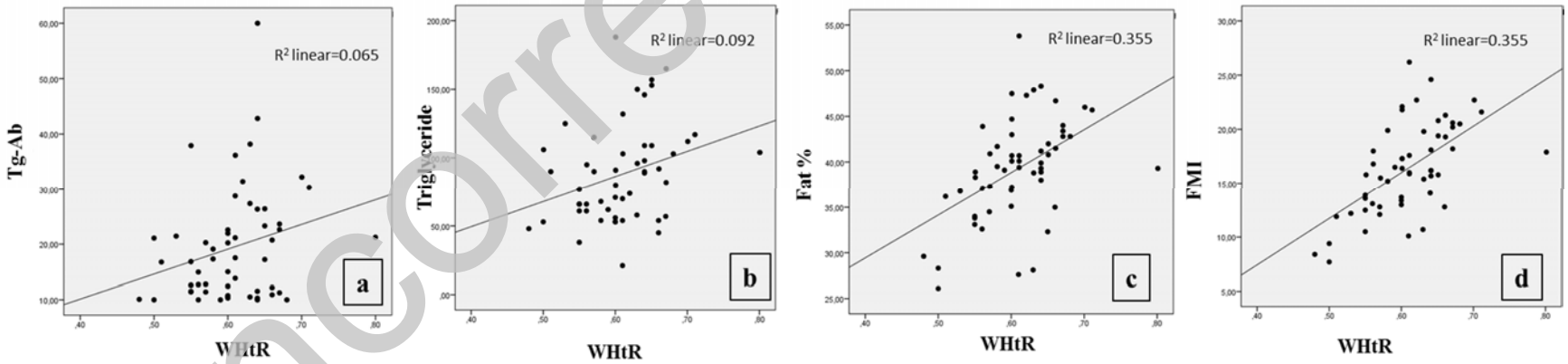

Table 1: Comparison of anthropometric measurements, metabolic parameters, thyroid function test and autoantibody levels between the obese and control group.

		Obese group (n=55)	Control group (n=38)	
Variable		**Mean±SDS Median (IQR) (min-max)**	**Mean±SDS Median (IQR) (min-max)**	**P**
Age, year		12.6±2,6 (7.1-17.3)	12±2.7 (7.3-17.5)	0.25*
Gender	Female	26 (%28)	19 (%20)	0,796**
	Male	29 (%32)	19 (%20)	
Puberty	Prepubertal	11 (%12)	9 (%10)	0,67**
	Pubertal	44 (% 47)	29 (% 31)	
Weight (kg)		76 (29.5) (31.2-122.9)	42.7 (24.1) (23-65)	**<0.001****
Weight SDS		2.82 (1.17) (0.94-4.46)	-0.12 (1.44) (-1.23-1.18)	**<0.001****
Height (cm)		158,7±13.7 (125-188)	149.8±15 (123.8-175)	**0.004***
Height SDS		0.86±1.1 (-1.52-4.12)	0.01±0.9 (-1.74-1.72)	**<0.001***
BMI		29.9 (7.2) (20-37.2)	18.7 (5.2) (14.3-23.9)	**<0.001****
BMI SDS		2.59 (0.81) (1.65-3.65)	-0.11 (1.44) (-1.83-1.14)	**<0.001****
BMI %		99.5 (1.5) (95.1-99.9)	44 (52) (3.5-84)	**<0.001****
fT3, pg/dL		4.02 (0.96) (1.0-6.23)	3.13 (0.96) (1.19-4.96)	**<0.001****
fT4, ng/dL		1.02±0.14 (0.71-1.39)	1.15±0.16 (0.81-1.52)	**<0.001***
TSH, IU/L		2.01 (1.06) (0.74-4.62)	1.46 (0.74) (0.51-4.18)	**<0.001****
TPO-ab, IU/mL		13 (10) (5-29)	7 (6) (5-20)	**<0.001****
Tg-ab, IU/mL		17 (12) (10-60)	15 (7) (8-26)	0.19***
Fasting glucose, mg/dL		90 (9) (66-100)	92 (6) (71-100)	0.81***
Fasting insulin, uU/mL		19 (13.5) (2.4-88.3)	8.1 (5.8) (1-20.6)	**<0.001****
HOMA-IR		4.6 (3.4) (0.56-17.9)	1.9 (1.3) (0.7-3.22)	**<0.001****
Triglyceride, mg/dL (n=88)		86 (50)	78 (46)	0.09***

	(21-188)	(18-169)	
HDL-C, mg/dL (n=88)	50 (14) (29-83)	60 (25) (4-84)	0.113***
LDL-C, mg/dL (n=88)	93 (31) (48-187)	82 (35) (41-110)	**0.036*** **
Cholesterol, mg/dL (n=88)	162 (40) (119-255)	150 (35) (106-178)	**0.041*** **
AST, IU/L (n=91)	20 (6) (11-45)	22 (6) (12-31)	0.429***
ALT, IU/L (n=91)	17 (12) (8-79)	15 (7) (7-25)	**0.001*** **

*: T-test, **: Chi-square test, ***: Mann-Whitney test

ALT: alanine aminotransferase, AST: aspartate aminotransferase, BMI: Body mass index, BMI SDS: Body mass index standard deviation-score, fT4: free thyroxine, fT3: free triiodothyronine, HDL-C: high-density lipoprotein cholesterol, HOMA-IR: homeostasis model assessment of insulin resistance, LDL-C: Low-density lipoprotein cholesterol, min-max: minimum-maximum,Tg-ab: thyroglobulin antibody; TPO-ab: thyroid peroxidase antibody, TSH: thyroid stimulating hormone

Table 2: Comparison of anthropometric measurements, metabolic parameters, thyroid function test and autoantibody levels between the WHtR ≤0.6 and WHtR >0.6 subgroups.

		WHtR ≤0.6 (n=27) (min-max)	**WHtR >0.6 (n=28) (min-max)**		**OR(%95 CI)**
Variable		**Mean±SDS Median (IQR)**	**Mean±SDS Median (IQR)**	**P**	
Age, year		12±2.7 (7.1-15.8)	13.3±2.4 (9.3-17.3)	0.054*	
Gender	Female	12 (%22)	14 (%25.5)	0.68**	
	Male	15 (%27)	14 (%25.5)		
Puberty	Prepubertal	6 (%11)	5 (%9)	0,686**	
	Pubertal	21 (%38)	23 (%42)		
Weight (kg)		69.4 (31.1) (31.2-111.3)	85.5 (30.5) (56-122.9)	**0.011****	
Weight SDS		2.37 (1.7) (0.94-4.34)	2.95 (0.8) (1.5-4.46)	0.083***	
Height (cm)		156.1±15.3 (125-186)	161.1±11,8 (142.2-188)	0.183*	
Height SDS		1.08±1.28 (-1.52-4.12)	0.65±0.9 (-1.35-2.15)	0.152*	
BMI		27.3 (4.6) (20-35.8)	32.9 (5.6) (26.7-37.2)	**<0.001****	
BMI SDS		+2.2 (0.78) (1.65-3.48)	+2.83 (0.5) (1.98-3.65)	**0.001****	
BMI %		99.6 (1.5) (95.1-99.9)	99.8 (0.6) (97.6-99.9)	**0.001****	
fT3, pg/dL		4.02 (1.04) (1.0-6.23)	4,05 (0.86) (1-5.74)	0.395***	
fT4, ng/dL		1.01±0.15 (0.77-1.34)	1.04±0.13 (0.71-1.39)	0.55*	
TSH, IU/L		1.96 (0.88) (1.24-4.01)	2.03 (1.46) (0.74-4.62)	0.655***	
TPO-ab, IU/mL		11 (8) (5-29)	16 (10) (6-25)	**0.023****	**0.262**
Tg-ab, IU/mL		13 (10) (10-38)	22 (18) (10-60)	**0.009****	**0.275**
Fasting glucose, mg/dL		92 (10) (80-100)	89 (10) 66-100)	0.269***	
Fasting insulin, uU/mL		17.7 (10) (2.4-39.8)	26.7 (14.3) (6.5-88.3)	**0.029****	
HOMA-IR		3.9 (2) (0.56-8)	5.7 (3.9) (1.5-17.9)	0.076***	
Triglyceride, mg/dL (group 1 n=26) (group 2 n=26)		66 (36) (38-188)	98 (47) (21-165)	**0.019****	

HDL-C, mg/dL (group 1 n=26) (group 2 n=26)	51 (17) (35-83)	49 (13) (29-71)	0.213***
LDL-C, mg/dL (group 1 n=26) (group 2 n=26)	95 (30) (48-187)	92 (34) (67-146)	0.833***
Cholesterol, mg/dL (group 1 n=26) (group 2 n=26)	164 (43) (119-255)	159 (35) (128-213)	0.184***
AST, IU/L (group 1 n=26) (group 2 n=28)	19 (6) (12-45)	21 (7) (11-40)	0.728***
ALT, IU/L (group 1 n=26) (group 2 n=28)	15 (9) (9-79)	22 (14) (8-42)	0.112***
Fat%	37.3±5 (26.1-47.5)	41.1±5.5 (27.6-53.8)	**<0.001***
FMI	14.5±3.6 (7.7-22.1)	18.2±3.9 (10.1-26.2)	**<0.001***

*: T- test, **: Chi-square testi, ***: Mann-Whitney test

ALT: alanine aminotransferase, AST: aspartate aminotransferase, BMI: Body mass index, BMI SDS: Body mass index standard deviation-score, Fat%: Fat mass/weight ratio, FMI: Fat mass index, fT4: free thyroxine, fT3: free triiodothyronine, HDL-C: high-density lipoprotein cholesterol, HOMA-IR: homeostasis model assessment of insulin resistance, LDL-C: Low-density lipoprotein cholesterol, min-max: minimum-maximum, Tg-ab: thyroglobulin antibody; TPO-ab: thyroid peroxidase antibody, TSH: thyroid stimulating hormone, WHtR: Waist/height ratio