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Thyroid Function in Obese Children and Adolescents and Its Association with Anthropometric and Metabolic Parameters

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Abstract

Fat accumulation leads to dysfunction of hypothalamic-pituitary-thyroid axis and to changes in thyroid function. A higher serum level of thyroid stimulating hormone (TSH), with normal levels of thyroid hormones, suggesting subclinical hypothyroidism, is often found in obese individuals. The influence on lipid and glucose metabolism of thyroid dysfunction in obese patients remains unclear. This retrospective study encompassed 110 obese children and 38 healthy non-obese children aged 5–18. Anthropometric measurements, including bioelectrical impedance, were taken in all children. Fasting TSH, fT4, glucose, lipid profile, and a glucose tolerance test in case of the obese individuals, were evaluated. The obese children demonstrated a significantly higher mean concentration of TSH compared with their peers with proper body weight: 2.1 ± 1.0 μIU/ml *vs*. 1.5 ± 0.6 μIU/ml, $p = 0.001$. The fT4 was not different between the two groups. In the obese children, TSH correlated with body mass index (BMI) and waist circumference after controlling for age and gender. A multivariate regression analysis showed a relationship of TSH with total cholesterol, LDL cholesterol, triglycerides, and non-HDL after adjusting for BMI. None of these relationships were revealed for fT4. The level of TSH correlated with the degree of abdominal obesity. We conclude that the serum TSH concentration, even remaining within the norm, could adversely affect the lipid profile, irrespective of obesity.

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1 Introduction

The evaluation of thyroid function is commonly conducted to determine the cause of obesity in children and adolescents. Numerous studies have shown that obese children have a higher concentration of the thyroid-stimulating hormone (TSH), compared with their non-obese peers, TSH correlates positively with body mass index (BMI) and the degree of obesity expressed by BMI SDS (standard deviation score) (Wolters et al. 2013; Longhi and Radetti 2013; Bastemir et al. 2007; Reinehr et al. 2006, 2008). Hyperthyreotropinemia with normal serum free thyroxine (fT4) and a normal or slightly elevated level of free triiodothyronine (fT3) is a common abnormality of thyroid function, more frequently observed in obese children than in the general population. Subclinical hypothyroidism, resulting from an autoimmune process, is rare in obese children (Ghergherehchi and Hazhir 2015).

The mechanisms underlying thyroid axis dysfunction are not yet fully understood. Several hypothesis have been proposed suggesting that thyroid dysfunction is a consequence of excess body weight rather than its cause. It is believed that dysfunction of the hypothalamic-pituitary-thyroid axis may have to do with nutritional status. To this end, leptin, a hormone produced by fat cells seems of importance. Leptin stimulates TSH production by a direct effect on the gene for the thyrotropin-releasing hormone (TRH). In addition, leptin influences the production of neurotransmitters and hormones in the arcuate nucleus, which target TRH neurons, such as neuropeptide Y, agouti-related protein, and alpha-melanocyte-stimulating hormone. Elevated TSH levels are explained by the presence of disturbed negative feedback, pituitary resistance to thyroid hormones due to a small number of T3 receptors in the hypothalamus, and a decreased activity of type 2 deiodinase in the pituitary gland caused by leptin. Increased activity of the 5-deiodinase, which is an expression of the body adaptation to increased resting energy expenditure and body protection from storing energy, facilitates enhancement of fT3 or T3 levels in obese subjects. Obesity is associated with a low grade inflammation. Pro-inflammatory cytokines, such as tumor necrosis factor alfa (TNF-α), interleukin 1 (IL-1), and interleukin 6 (IL-6) secreted into the bloodstream inhibit sodium/iodide symporter mRNA expression and iodine uptake in thyrocytes, which may lead to a compensatory rise of TSH (Lobotková et al. 2014; Santini et al. 2014; Longhi and Radetti 2013; Pacifico et al. 2012; Reinehr 2010).

The role of thyroid hormones in the regulation of basal metabolism, energy homeostasis, fat oxidation, and lipid and carbohydrate metabolism is well known. However, the effect on metabolic status of obesity-related thyroid dysfunction is the cause of much controversy. The results of previously published studies are inconsistent (Pacifico et al. 2012; Reinehr 2010). The aim of this study was to evaluate thyroid function in the context of glucose and lipid metabolism in children with simple obesity and to compare it with that present in healthy peers.

2 Methods

The Bioethics Committee of Medical University of Warsaw approved the study. We conducted a retrospective analysis based on the medical history of 110 obese children (48 girls, 62 boys) and 38 healthy, non-obese children (21 girls, 17 boys), aged 5–18 years hospitalized in the

Department of Pediatrics and Endocrinology of the Medical University of Warsaw in the years 2010–2012. All of the children were non-smokers and did not take any medication. A history of endocrine or systemic inflammatory disorders and hereditary diseases was negative. They did not have symptoms typical of thyroid dysfunction. Obesity was defined as Body Mass Index (BMI) over the 97th percentile according to the criteria of International Obesity Task Force (IOTF) (Cole et al. 2000). To normalize the BMI's skewed distribution, we used the Cole least mean square method (Cole 1990) consisting of the calculation of the standard deviation score of BMI (SDS BMI) to express the degree of obesity.

2.1 Anthropometric Measurements

Body weight (kg), standing height (cm), waist circumference (WC) and hip circumference (cm), and thickness of skinfolds (mm) on the shoulder above the triceps and under the right lower angle blades were measured. The measurements of waist and hip circumference was made according to the WHO recommendations (WHO Expert Committee 1995). Based on the measurements of the two skinfolds, the body fat percentage (%FAT) was calculated using the Slaughter equation (Slaughter et al. 1998). Additionally, the body composition of the obese children was assessed with the bioelectrical impedance analysis (BIA) using a Maltron Body Fat Analyzer (BF-905; Maltron International, Rayleigh, UK). The results of these measurements were used to calculate waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR).

2.2 Laboratory Analysis

Blood for thyroid hormones (TSH, fT4), lipids profile, and glucose was taken in the fasting state in all the children. In the obese children, glucose and insulin were measured using oral the glucose tolerance test (OGTT). TSH (μIU/ml) and fT4 (ng/dl) concentrations were determined by a microparticle immunoenzymatic MEIA assay (Abbott; Longford, Ireland) using AXYM analyzer (Abbott; Longford, Ireland). The reference range for TSH was 0.4–5.0 μIU/ml and for fT4 was 0.6–1.4 ng/dl. In children with TSH levels >4 μIU/ml, thyroid autoantibodies (antithyroidal peroxidase – TPO-Ab, and thyreoglobulin antibodies – Tg-Ab) were evaluated and thyroid ultrasound scans were performed to exclude autoimmune thyroiditis. Glucose (mg/dl), insulin (μIU/ml), total cholesterol (TC, mg/dl), high-density lipoprotein cholesterol (HDL-C, mg/dl), and triglyceride (TG, mg/dl) concentrations were measured using commercially available tests. Low-density lipoprotein cholesterol (LDL-C, mg/dl) was calculated using the Friedewald formula in children with TG concentration lower than 400 mg/dl, non-HDL cholesterol was calculated according to the formula: non-HDL = TC – HDL-C (Srinivasan et al. 2006). Homeostasis model assessment [HOMA = (insulin μIU/ml × glucose mmol/l)/22.5] was used to evaluate the degree of insulin resistance (Ten and Maclaren 2004).

2.3 Statistical Analysis

Data were presented as means ± SE or means ± SE, as indicated. Statistically significant differences between the groups were examined by means of a *t*-test or variation analysis for normally distributed parameters and by Mann–Whitney *U* test for non-normal distribution. Associations between variables were tested by Spearman's coefficient correlation. Multiple linear regression analysis models were used for more reliable assessment of relationships between TSH and fT4, and chosen anthropometric, carbohydrate, and lipid parameters related to obesity, after controlling for age and gender. A p-value <0.05 was considered statistically significant. Statistical analysis was performed using SPPS 19 software.

3 Results

Anthropometric and biochemical characteristics of obese and non-obese children are presented in Table 1. The obese children demonstrated significantly higher mean concentrations of TSH compared with their peers with proper body weight: 2.1 ± 1.0 μIU/ml *vs.* 1.5 ± 0.6 μIU/ml, $p < 0.001$ (Fig. 1). The mean levels of TSH increased with increasing SDS BMI (Fig. 2). The scatter of TSH values was substantial; from 0.44 μIU/ml to a maximum of 4.90 μIU/ml. In five obese children with TSH levels of more than 4.00 μIU/ml, the evaluation of thyroid autoantibodies and thyroid ultrasound scans excluded autoimmune thyroiditis. The mean concentration of fT4 did not differ between the obese and non-obese groups (1.0 ± 0.2 ng/dl *vs.* 1.0 ± 0.1 ng/dl, respectively, $p = 0.589$). In all patients, serum fT4 level was within the reference range (minimum 0.06 ng/dl, maximum 1.64 ng/dl). The TSH value did not correlate with fT4.

In the obese and non-obese children taken together, serum TSH values correlated with age ($r = -0.305$, $p < 0.001$), SDS BMI ($r = 0.333$, $p < 0.001$), WHR ($r = 0.326$, $p < 0.001$), and WHtR ($r = 0.282$, $p = 0.001$). The association between TSH and BMI demonstrated a borderline significance ($r = 0.150$, $p = 0.071$). The FT4 level correlated with age ($r = -0.246$, $p = 0.003$), body weight ($r = -0.213$, $p = 0.013$), and the hip circumference ($r = -0.194$, $p = 0.024$). In the multivariate regression analysis with TSH, as a dependent variable, and the independent variables describing weight status (BMI, SDS BMI, WC, WHR, WHtR, and % FAT) after controlling for age and gender, TSH significantly correlated with BMI, SDS BMI, and WC (Table 2). None of the above associations was found for fT4. There was a trend for the association between TSH and the percentage of lean body mass (% LEAN) in obese children ($r = 0.174$, $p = 0.071$), but not the percentage of fat mass ($p = 0.101$) as estimated with bioelectrical impedance analysis.

Concerning the associations between serum TSH and fT4 and glucose and lipid metabolism, we found a significant association of TSH with TC ($r = 0.364$, $p < 0.001$), LDL-C ($r = 0.333$, $p < 0.001$), TG ($r = 0.280$, $p = 0.001$), and non-HDL ($r = 0.386$, $p < 0.001$), but not with HDL cholesterol ($r = -0.109$, $p = 0.194$).

Table 1 Anthropometric and biochemical parameters in obese and non-obese children

Variable	Obese	Non-obese
Age (year)	11.5 ± 2.9	13.4 ± 2.6***
Height (cm)	153.8 ± 16.4	157.5 ± 12.9
Body weight (kg)	71.6 ± 23.9	46.9 ± 13.3***
Body mass index (kg/m^2)	29.4 ± 4.9	16.8 ± 2.8***
SDS BMI	2.78 ± 0.49	−0.03 ± 0.89***
Waist circumference (cm)	89.9 ± 12.3	64.2 ± 6.7***
Hip circumference (cm)	101.0 ± 14.0	82.9 ± 10.7***
WHR	0.89 ± 0.06	0.78 ± 0.05***
WHtR	0.58 ± 0.05	0.41 ± 0.02***
% FAT (skinfold)	33.9 ± 4.7	20.3 ± 6.4***
Fasting glucose (mg/dl)	84.0 ± 10.6	82.0 ± 10.2
TC (mg/dl)	177.5 ± 29.5	156.8 ± 23.9***
HDL-C (mg/dl)	44.0 ± 10.8	55.9 ± 12.5***
LDL-C (mg/dl)	106.3 ± 27.2	84.3 ± 25.6***
TG (mg/dl)	135.3 ± 63.4	77.1 ± 35.9***
non-HDL (mg/dl)	133.4 ± 30.9	100.9 ± 2***
%FAT (BIA)	38.1 ± 8.2	–
%LEAN (BIA)	61.8 ± 8.4	–

Data are means ± SD

WHR waist-to-hip ratio, *WHtR* waist-to-height ratio, *%FAT* % of fat mass, *%LEAN* % lean body mass, *BIA* bioelectric impedance analysis, *TC* total cholesterol, *TG* triglycerides, *HDL-C* HDL cholesterol, *LDL-C* LDL cholesterol

***$p < 0.001$

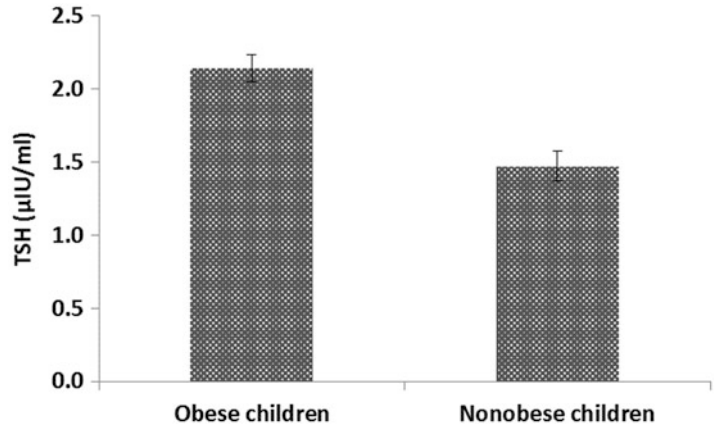

Fig. 1 TSH serum concentration in obese and non-obese children. Data are means ± SE

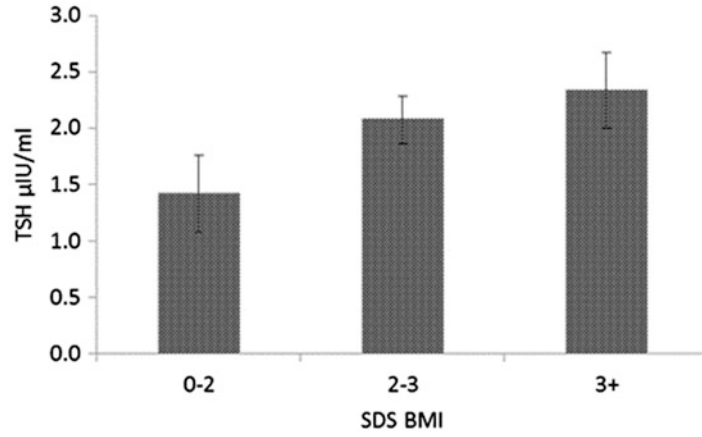

Fig. 2 TSH serum concentration in children according to the standard deviation score of body mass index (SDS BMI). Data are means ± SE; $p < 0.05$ (0–2 *vs*. 2–3 and 0–2 *vs*. 3+)

Table 2 Multivariate regression of anthropometric parameters (independent variables) on TSH serum concentration (dependent variable) after controlling for age and gender

Independent variables	B	SE	p-value
Age	−0.112	0.026	0.001
Gender	0.160	0.147	0.280
BMI	0.033	0.012	0.005
Age	−0.089	0.025	0.001
Gender	0.208	0.147	0.159
SDS BMI	0.097	0.033	0.004
Age	−0.118	0.027	0.001
Gender	0.056	0.153	0.716
WC	0.013	0.005	0.016
Age	−0.065	0.028	0.022
Gender	−0.025	0.161	0.878
WHR	3.155	1.223	0.011

BMI body mass index, *SDS BMI* standard deviation score of body mass index, *WC* waist circumference, *WHR* waist-to-height ratio, *B* non-standardized coefficient, *SE* standard error

Similar results to those outlined above were obtained in the multivariate regression analysis of TSH, along with age and gender, as an independent variable on the lipid profile. Total cholesterol, LDL cholesterol, triglycerides and non-HDL correlated with TSH, even after controlling for BMI or SDS BMI (Table 3). None of these associations were revealed for fT4. Thyroid variables did not correlate with glucose and insulin levels measured under fasting condition or during OGTT, or with the insulin resistance index HOMA.

4 Discussion

Thyroid function in obese children and adolescents seems of increasing medical interest lately. The most frequent change is an increase in

Table 3 Multivariate regressions of TSH (independent variable) on serum lipid concentrations after controlling for age, gender, and obesity (dependent variables)

Dependent variable	Independent variables	B	SE	p-value
TC	TSH (+BMI)	9.126	2.924	0.002
	TSH (+SDS BMI)	9.204	2.901	0.002
LDL-C	TSH (+BMI)	5.768	2.735	0.038
	TSH (+SDS BMI)	5.891	2.721	0.033
TG	TSH (+BMI)	15.054	6.204	0.017
	TSH (+SDS BMI)	14.690	6.222	0.020
HDL-C	TSH (+BMI)	0.405	1.104	0.714
	TSH (+SDS BMI)	0.433	1.098	0.694
non-HDL	TSH (+BMI)	8.721	3.092	0.006
	TSH (+SDS BMI)	8.771	3.080	0.005

TC total cholesterol, *LDL-C* LDL cholesterol, *HDL-C* HDL cholesterol, *TG* triglycerides, *B* non-standardized coefficient, *SE* standard error

TSH level, which is considered to be an adaptive process to excess body mass (Pacifico et al. 2012; Reinehr 2010). In the present study we confirmed typical changes in thyroid function in obese children and we searched for associations correlations between TSH and fT4, and anthropometric and metabolic parameters. We found that the TSH level in obese patients was higher than that in their peers with normal weight, but the serum fT4 level was comparable between the two groups. Some studies have reported that obese children have a slightly elevated or normal serum triiodothyronine (T3) and free triiodothyronine (fT3) (Lobotkova et al. 2014; Wolters et al. 2013; Marras et al. 2010; Reinehr et al. 2006). In our present study, fT3 was not measured, which might be seen as certain limitation of our assessment of thyroid function. However, all of our obese patients had normal serum TSH and fT4, which made us deem the additional evaluation of fT3 unwarranted. Nevertheless, in five children with the serum TSH above 4.0 μIU/ml additional tests were conducted, but they failed to reveal autoimmune thyroiditis. In the literature, prevalence of isolated hyperthyreotropinemia is estimated to be between 15 % (Ghergherehchi and Hazhir 2015) and 23 % (Reinehr et al. 2008), which in most cases is not associated with a thyroid disease. In the study by Radetti et al. (2008) in 186 overweight and obese children, antithyroid antibodies were not found in 76.8 % of patients, with a normal ultrasound image pattern in 39.2 % of them. In the remaining patients, ultrasound images showed autoimmune thyroiditis, but without typical morphological changes in fine needle aspiration cytology. These equivocal findings were explained by the existence of low-grade inflammation related to obesity. In the above quoted work, thyroid antibodies were found only in 23.2 % of overweight and obese children, and 12.4 % of them demonstrated ultrasound image alterations suggestive of Hashimoto's thyroiditis.

Thyroid hormones play a role in promoting thermogenesis and energy expenditure. Thus, relationship between thyroid disorders and body weight gain and obesity is of research interest. In most studies, serum TSH concentration positively associates with BMI or SDS BMI (Aeberli et al. 2010; Grandone et al. 2010; Marras et al. 2010; Reinehr et al. 2008; Bastemir et al. 2007; Knudsen et al. 2005). This association was affirmed in the present work when the obese and non-obese children were pooled. Several studies show that thyroid function abnormalities observed in obese patients usually normalize after weight reduction (Wolters et al. 2013; Grandone et al. 2010; Reinehr et al. 2006), suggesting that thyroid dysregulation reflects an adaptive process to weight excess. The relationship of TSH level to anthropometric parameters describing abdominal obesity, confirmed in the present study, might indirectly suggest an association between leptin and increased TSH. Aeberli et al. (2010) have suggested that a link between leptin and serum

TSH concentration in obese children is independent of body weight and fat. Moreover, in patients with overt hypothyroidism a slight body weight gain is not associated with excess of fat mass, as it might seem, but with the tissue accumulation of water-binding glycosaminoglycans. Loss of body weight after LT4 replacement therapy is a result of excretion of excess water and a decrease in lean body mass as demonstrated in the examination of body composition using dual-energy X ray absorptiometry (Laurberg et al. 2012). In the present study, we observed a trend for the association between TSH and the percentage of lean body mass, and not of fat mass, in obese children as assessed in bioelectrical impedance body fat analysis. That observation is confirmatory to the notion that thyroid hormones influence body weight mainly through changes in the water compartment. In this context, it is worth mentioning a study of Matusik et al. (2015) who have investigated 51 obese children with isolated hyperthyreotropinemia participating in a combined dietary-behavioral-physical activity intervention. There were 25 individuals who took levothyroxine (LT4) treatment among the children. The authors found that LT4 therapy does not help reduce BMI.

The influence on lipids and carbohydrate metabolism in obesity of thyroid function is under investigation. Observational studies suggest a propensity for increased risk of atherogenic lipids, insulin resistance, hypertension, and endothelium dysfunction in subclinical hypothyroidism (Gierach et al. 2014; Pearce 2012). There are a few general population studies demonstrating a relationship between adverse changes in the lipid profile and increasing TSH concentration, even when it remains within the normal range; as having been found in a 11-year follow-up (Asvold et al. 2007, 2013). The clinical relevance of these relationships in obese children remains unclear. In a prospective study in 206 obese children, Aeberli et al. (2010) have shown a relationship between TSH, but not fT4 or fT3, and total cholesterol (TC), low–density lipoprotein cholesterol (LDL-C) and triglycerides (TG). During a 2-month weight loss intervention, changes in TSH were good predictors of the corresponding changes in high-density lipoprotein cholesterol (HDL-C). Likewise, Pacifico et al. (2012) have shown that elevated TSH is a predictor of lipid and glucose disorders, and also hepatic steatosis. In contrast, Reinehr et al. (2006) and Grandone et al. (2010) in multiple regression analysis adjusted for age, gender, pubertal stage, degree of weight and HOMA of 246 and 938 obese children, respectively, have failed to substantiate the existence of associations between TSH, fT4, fT3, and lipid metabolism. Further, improvement in the lipid profile due to weight reduction was not associated with a change in the level of thyroid hormones after adjustment for BMI. In the present study, TSH level, being within the normal range, correlated with TC, LDL-C, and TG, irrespective of BMI or SDS BMI in the whole group, which is in line with a report of Aeberli et al. (2010). We also found an association between TSH and non-HDL cholesterol which is a well-established marker of subclinical atherogenesis, as it reflects the concentration of all atherogenic lipoproteins and closely correlates with that of apolipoprotein B (ApoB) (Srinivasan et al. 2006).

Studies regarding the influence of thyroid hormonal derangements on obesity-related glucose metabolism and insulin resistance are also controversial. Bastemir et al. (2007) have examined a group of 350 obese children and found a relationship between serum TSH concentration and fasting insulin and HOMA-IR. That has been confirmed by Aeberli et al. (2010) who found that decreases in TSH concentration predicted decreases in fasting insulin and HOMA, irrespective of changes in body weight or composition. These authors, however, failed to substantiate any association between TSH, fT4, fT3 and the glucose level during the OGTT. On the other side, Garduno-Garcia et al. (2015) have found a negative association between fT4, but not TSH, and HOMA and insulin concentration during OGTT in a group of healthy adolescents with risk factors for diabetes, who were enrolled into a 2-month weight loss program. In the present study, serum TSH and fT4 levels were not associated with glucose

and insulin metabolism. The absence of such associations between TSH, fT4, fT3 and insulin and HOMA has been confirmed in a cross-sectional and longitudinal analysis by Reinehr et al. (2008). Nor have any associations been found between thyroid function and fasting glucose or insulin concentration in a study of Marras et al's (2010) either.

5 Conclusions

Changes in thyroid function, suggesting subclinical hypothyroidism, are consistently found in obese patients. In the present study, obese children and adolescents had a higher TSH serum concentration, even when it remained within the normal range, compared to their peers with proper weight. The level of TSH positively correlated with the anthropometric parameters describing abdominal obesity, but the role of TSH in the accumulation of fat mass is unclear. The study findings suggests that TSH could contribute to increases in total cholesterol, LDL lipoprotein cholesterol, triglycerides, and non-HDL, independently of obesity. Enhanced, or merely being persistently on the high side, serum TSH concentration should plausibly be taken into account as a potential detriment of lipid metabolism in obese children. Clinical significance of this association should be explored in further research.

References

Aeberli I, Jung A, Murer SB, Wildhaber J, Wildhaber-Brooks J, Knopfli BH, Zimmermann MB (2010) 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 95:5412–5418

Asvold BO, Vatten LJ, Nilsen TIL, Bjoro T (2007) The association between TSH within the reference range and serum lipid concentration in a population – based study. The HUNT Study. Eur J Endocrinol 156:181–186

Asvold BO, Bjoro T, Vatten LJ (2013) Associations of TSH levels within the reference range with future blood pressure and lipids concentrations: 11- years follow – up of the HUNT Study. Eur J Endocrinol 169:73–82

Bastemir M, Akin F, Alkin E, Kaptanoght B (2007) Obesity is associated with increased serum TSH level, independent of thyroid function. Swiss Med Wkly 137:431–434

Cole TJ (1990) The LMS method for constructing normalized growth standard. Eur J Clin Nutr 44:45–60

Cole TJ, Bellizzi MC, Flegal KM (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 320:1240–1243

Garduno-Garcia J, Romero EC, Ochoa AL, Romero-Figueroa S, Bravo GH, Garcia RT, Montenegro-Morales P, Mendieta-Zeron GH (2015) Thyroid function is associated with insulin resistance markers in healthy adolescents with risk factors to develop diabetes. Diabetol Metab Syndr 7:16

Ghergherehchi R, Hazhir N (2015) Thyroid hormonal status among children with obesity. Ther Adv Endocrinol Metab 6(2):51–55

Gierach M, Gierach J, Jumnik R (2014) Insulin resistance and thyroid disorders. Endokrynol Pol 65:70–76

Grandone A, Santoro N, Copploa F, calabro P, Perrone L, Giudoce EM (2010) Thyroid function defragment and childhood obesity: an Italian experience. BMC Endocr Disord 10:1–8

Knudsen N, Lauberg P, Rasmussen LB, Bülow I, Perrild H, Ovesen L, Jorgensen T (2005) Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. J Clin Endocrionol Metab 90 (7):4019–4024

Laurberg P, Knudsen N, Andersen S, Carle A, Bulow Pedersen I, Karmisholt J (2012) Thyroid function and obesity. Eur Thyroid J 1:159–167

Lobotková D, Staníková D, Staník J, Cervenová O, Bzdúch V, Tichá L (2014) Lack of association between peripheral activity of thyroid hormones and elevated TSH levels in childhood obesity. J Clin Pediatr Endocrinol 6:100–104

Longhi S, Radetti G (2013) Thyroid function and obesity. J Clin Pediatr Endocrinol 5(Suppl 1):40–44

Marras V, Casini MR, Pilia S, Carta D, Civolani P, Porcu M, Uccgeddu AP, Loche S (2010) Thyroid function in obese children and adolescents. Horm Res Paediatr 73:193–197

Matusik P, Gawlik A, Januszek-Trzciakowska A, Malecka-Tendera E (2015) Isolated subclinical hyperthyrotropinemia in obese children: does levothyroxine (LT4) improve weight reduction during combined behavioral therapy? Int J Endocrinol 2015:792509. doi:10.1155/2015/792509

Pacifico L, Anania C, Ferraro F, Andreoli GM, Chiesa C (2012) Thyroid function in childhood obesity and metabolic comorbidity. Clinica Chimica Acta 413:396–405

Pearce EN (2012) Update in lipids alterations in subclinical hypothyroidism. J Clin Endocrinol Metab 97:326–333

Radetti G, Kleon W, Buzi F, Crivellaro C, Pappalardo L, Maghnie N, Maghnie M (2008) Thyroid function and structure are effected in childhood obesity. J Clin Endocrinol Metab 93:4749–4754

Reinehr T (2010) Obesity and thyroid function. Mol Cell Endocrinol 316:165–171

Reinehr T, de Sousa G, Andler W (2006) Hyperthyrotropinemia in obese children is reversible after weight loss and is not related to lipids. J Clin Endocrinol Metab 91:3088–3091

Reinehr T, Isa A, de Sousa G, Dieffenbach R, Andler W (2008) Thyroid hormones and their relationship to weight status. Horm Res 70:51–57

Santini F, Marzullo P, Rotondi M, Ceccarini G, Pagano L, Ippolito S, Chiovato L, Biondi B (2014) The crosstalk between thyroid glan and adipose tissue: signal integration in health and disease. Eur J Endocrinol 171:8137–8152

Slaughter MH, Lohman TG, Christ CB, Boileau RA (1998) Skinfold equations for estimation of body fitness in children and youth. Hum Biol 60:709–723

Srinivasan SR, Frontini MG, Xu J, Berenson GS (2006) Utility of childhood non – high- density lipoprotein cholesterol levels in predicting adult dyslipidemia and other cardiovascular risks: the Bogalusa Heart Study. Pediatrics 118:201–206

Ten S, Maclaren N (2004) Insulin resistance syndrome in children. J Clin Endocrinol Metab 89(6):2526–2539

WHO Expert Committee (1995) Physical status: the use and interpretation of anthropometry, WHO technical report series 854. WHO, Geneva

Wolters B, Lass N, Reinehr T (2013) TSH and free triiodothyronine concentrations are associated with weight loss in a life style intervention and weight regain afterwards in obese children. Eur J Endocrinol 168:323–329