

Relationship between thyroid stimulating hormone and metabolic syndrome in overweight/obese children

Original Article

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Abstract:

Background: Background: Obesity, especially central obesity is related to many endocrine abnormalities, such as thyroid dysfunctions. Elevated levels of thyroid stimulating hormone (TSH) is common in obese children, however, it is not clear if such condition is associated with increased cardiovascular risk factors. The study aimed to determine the association between levels of TSH in overweight and obese children with components of metabolic syndrome (Mets).

Methods: The study sample included 197 overweight/obese 6-7 year old children in Tehran, Iran. Anthropometric (weight, waist circumference and height), metabolic (high-density lipoprotein cholesterol, triglycerides and fasting blood glucose) and hormonal (TSH) variables, as well as blood pressure were measured. Mets was defined according to Cook definition.

Results: Totally, 20.3% and 79.7% of children were overweight and obese, respectively. Elevated levels of TSH were diagnosed in 10 subjects (5.1%), while Mets was seen in 35.4%. The most frequent component of Mets was abdominal obesity (72.5%). A weak positive correlation between BMI for age, Z scores and TSH level ($r = 0.11$, P value = 0.123) was observed only in girls ($r = 0.2$, P value = 0.034). TSH was not associated with components of Mets.

Conclusion: Elevated TSH levels may be found in obese children; however, the association between TSH elevation and cardiovascular disease risk factors, including components of metabolic syndrome needs further investigation.

Key Words: Hypothyroidism, Overweight, Metabolic Syndrome, Cardio Vascular Risk Factor

Citation:

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Introduction:

Childhood obesity is a worldwide health problem and its prevalence has increased from 4.2% in 1990 to 6.7% in 2010 and is expected to reach 9.1% or 60 million by 2020 ^[1]. In Iran, based on the latest report, the prevalence of overweight and obesity among school-age children is 7.9% and 5.6%, respectively ^[2]. Obesity is associated with an increased risk of chronic disease, metabolic syndrome (Mets) and all-cause mortality in children ^[3, 4]. There have been attempts to investigate different factors contributing to obesity. One of the factors that has been evaluated in this regard is thyroid function in obese children because the adverse effects of thyroid dysfunction on lipid profile, insulin sensitivity and other components of Mets (Cook et al. definition) ^[5] may lead to cardiovascular diseases. Obesity, especially central obesity is linked to many endocrine abnormalities, including thyroid dysfunctions ^[6, 7]. This is not surprising since triiodothyronine (T3) regulates energy metabolism, thermogenesis and plays a critical role in glucose and lipid metabolism, food intake and oxidation of fatty acids. It is well documented that hyperthyroidism can lead to weight loss and hypothyroidism is associated with

weight gain; however, changes in thyroid homeostasis occurring in obesity are controversial [8, 9]. Ozer et al. reported significantly higher TSH level in obese children with Mets as compared to their non-obese counterparts ($p = 0.045$) [10]. Several factors have been suggested as contributing to elevated thyroid stimulating hormone (TSH) levels in obesity, including iodine deficiency or autoimmune thyroiditis, derangement in the hypothalamic-pituitary axis and thyroid hormone resistance [11].

Elevated levels of TSH are common seen in obese children, but it is not clear whether such condition is associated with cardiovascular risk factors [12]. The aim of this study was to investigate the association between TSH level and components of Mets in overweight/obese children aged 6–7 years.

Methods:

The study was conducted as the baseline analysis of a primary health care-based trial on 197 overweight/obese 6-7-year-old students, under the coverage of 5 public health care centers in the city of Tehran. At the initial assessment, children with systemic disease, multiple endocrine disorders, epilepsy, history of medication and congenital or acquired hypothyroidism, as well as those on a special diet were excluded from the study. All subjects signed a written informed consent. The study protocol was approved by the ethics committee of the National Nutrition and Food Technology Research Institute (approval code: 4965-521 date: 10/24/2013).

Anthropometric measurement:

Weight, waist circumference (WC) and standing height were measured using standard methods [13]. Weight were measured on a Seca robusta 813, digital floor scale with children wearing light clothes and no shoes, and standing height was measured by Seca stadiometer with an accuracy of tenth of a centimeter. To measure waist circumference (WC), subjects were asked to stand relaxed with arms at the sides, feet positioned close together and weight evenly distributed across feet. WC was measured midway between the lowest rib and the superior border of iliac crest at the end of normal expiration with a stretch-resistant measuring tape. Body mass index (BMI) was calculated and Z scores of BMI for age were calculated by WHO AnthroPlus2007 software. Overweight was defined as BMI Z score ≥ 1 SD < 2 from the median and obesity as BMI Z score ≥ 2 SD more than the median for age and sex group based on WHO criteria [14].

Biochemical measurement:

After an overnight fast (at least 12 hours), 5 cc blood samples were obtained and serum levels of total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides and glucose were measured with the Roche Hitachi 717 Chemistry Analyzer. Results were expressed based on mg/dl. TSH was measured using an electrochemiluminescence immunoassay (Elecys 2010) method as screening for thyroid dysfunctions. The reference ranges for TSH were considered 0.6–5.1 for girls and 0.7–5.4 for boys [15]. Values above 5.1 IU/ml in girls and ≥ 5 IU/ml in boys were considered as elevated level. For those with TSH levels above 5 IU/ml, TSH measurement was repeated.

Blood pressure:

Blood pressure was measured by a trained physician in the health center using a standard sphygmomanometer (Aneroid, HS-20C, made in China) on the right arm with the child in the seated position after at least 15 min of rest and recorded as mmHg. All measurements were randomly overseen by study team.

Mets and its components, including hyperglycemia, hypertension, low level of HDL_C and elevated level of triglyceride were measured and defined according to Cook et al [5].

Statistical Analysis:

In order to compare qualitative variables, chi-square test was used. To compare the mean and standard deviations of components of Mets in children with normal and elevated TSH levels, ANCOVA adjusted for BMI Z-score was applied. Data were statistically analyzed using SPSS16. $P < 0.05$ was statistically considered significant.

Results:

The study sample included 92 boys and 105 girls with mean BMI of 21.24 ± 2.54 kg/m². Among them, 20.3% and 79.7% were overweight and obese, respectively. Frequency of overweight and obesity in girls was 21% and 79%, respectively, compared to 19.6% overweight and 80.4% obesity in boys ($p > 0.05$). In obese children, the mean and standard deviation of TSH levels were 2.92 ± 1.48 IU/ml, which was higher than those of overweight's (2.56 ± 1.29 IU/ml) but not significant. Elevated levels of TSH were observed in 5.1% of children. TSH levels of children based on their sex and weight status are presented in table 1.

Mets was seen in 35.4% of children. The most frequent component of Mets was abdominal obesity (72.5%). There was no abnormal glucose level. No significant correlation was observed between the components of Mets and levels of TSH (Table 2). BMI for age Z-score and TSH level were weakly associated with each other ($r=0.11$, P value= 0.123); however, this

relationship was only significant in girls ($r=0.2$, P -value= 0.034). Significant positive but weak correlation was found between TSH and WC ($r =0.14$, P -value= 0.047), which was not significant after adjusting for BMI for age Z-score. TSH levels were not correlated with lipid profile and FBS.

Table1. TSH level and weight status of overweight and obese children by gender

TSH level	Overweight n (%)			Obese n (%)			P value
	Girls	Boys	Total	Girls	Boys	Total	
Elevated*	1(100)	0(0)	1(100)	2(22.2)	7(70.0)	9(100)	
Normal	21(53.8%)	18(46.2%)	39(100)	81(54.7)	67(45.3)	148(100)	
P value	0.36			0.058			0.4

Chi-Square Test

* ≥ 5.1 IU/ml in girls, ≥ 5 IU/ml in boys

Table2. Comparison between mean and standard deviations of components of metabolic syndrome in children with normal vs. elevated TSH levels

Components of Metabolic Syndrome	TSH levels		P value*
	Elevated n=10 Mean \pm SD	Normal n=187 Mean \pm SD	
Waist circumference (Cm)	71.83 \pm 10.26	69.22 \pm 7.35	0.93
HDL (mg/dl)	42.75 \pm 7.83	40.69 \pm 9.41	0.39
Triglycerides (mg/dl)	101.25 \pm 36.49	92.7 \pm 38.7	0.72
FBS(mg/dl)	91.75 \pm 4.65	92.87 \pm 6.39	0.58
BP(systolic) (mmHg)	115 \pm 17.6	112.21 \pm 12.68	0.9
BP(diastolic) (mmHg)	75 \pm 10.48	69.79 \pm 11	0.43

*ANCOVA adjusted for BMI Z score

Discussion:

The results imply that elevation of TSH concentrations can be expected in obese children; however, it is not associated with Mets risk factors. Subclinical hypothyroidism was seen in children with obesity (14.7%) compared with normal subjects (6.8%, $p=0.02$) in Tabriz [16], as well as in Danish children (10.4% vs. 6.4%, $p=0.0001$) [17]. Due to not having a control group, we were unable to compare the results with normal weight children. In the present study, the frequency observed for elevated levels of TSH in obese children was much lower than that reported by Bouglé (5.1% vs. 13%) [18]. This can be attributed to different cutoff points, as well as study design.

In recent years, there has been an increasing focus on thyroid function in obese children and its association with components of Mets [10, 19]. Based on our findings, there was no association between serum TSH level and lipid profile, as well as FBS. There have

been some inconsistent and consistent studies with the present results, even with significant relationship between TSH and some parameters of lipid profile or other components of Mets [20-22]. In a study in Spain, no significant difference was observed between cardiovascular risk factors in children with elevated levels of TSH and those with normal levels [23]. Reinehr declared that lipids significantly did not correlate to thyroid hormones [24]. HDL_C levels are normal or even elevated in severe hypothyroidism because of decreased activity of Cholesteryl-Ester Transfer Protein and hepatic lipase, which are enzymes regulated by thyroid hormones [25]. Also, studies have shown that elevation of WC can alter TSH levels [26]. In the current study, WC was significantly associated with TSH level; however, this correlation was disappeared after controlling for BMI Z-scores. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI in adults, but it is not clear in pediatrics [27]. Obese children are at increased metabolic risk, because they can present insulin

resistance, hypertension or dyslipidemia [28]. We demonstrated that obese children with elevated TSH levels do not have an increase in their metabolic risk factors.

In conclusions, the results suggest that in obese children: (1) a moderate elevation of TSH concentrations may be found; (2) increase in TSH is not associated to metabolic risk factors. It is important for clinicians to check for alterations that occur in serum TSH and thyroid hormone values. Future studies should clarify whether the changes in TSH levels in obese children are cause or consequence of weight status and whether these subtle differences merit treatment with thyroxin.

The present study has some limitations. First, we did not measure leptin level which can affect TSH level. Thyroiditis should always be excluded when obese patients show elevated TSH levels. In the present study we did not assess thyroiditis. Lack of a control group (normal weight children) was another limitation. In addition, puberty stage which may affect the results was not evaluated. Also, our study design does not allow testing for any causal association between elevation of TSH and obesity.

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References:

1. De Onis M, Blössner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr* 2010; 92(5):1257-64.
2. Siassi F, Mohammad K, jazayery A, et al. National Integrated Micronutrient Survey 2012 (NIMS-2). Iran, Tehran: Ministry of Health and Medical Education; Andisheh Mandegar, Inc. 2015. [Text in Persian]
3. McCrindle BW. Cardiovascular consequences of childhood obesity. *Canadian J Cardiol* 2015; 31(2): 124-30.
4. Pulgaron ER. Childhood obesity: a review of increased risk for physical and psychological comorbidities. *Clin Ther* 2013; 35(1): A18-32.
5. Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. *Arch Pediatr Adolesc Med* 2003; 157(8): 821-7.
6. Krause A, Cines B, Pogrebniak E, et al. Associations between adiposity and indicators of thyroid status in children and adolescents. *Pediatr obes* 2016; 11(6): 551-8.
7. Jacob AS, Reetha G. Prevalence of metabolic comorbidities in obese children. *Inter J Contemp Pediatr* 2017; 4(4): 1450-5.
8. Reinehr T. Thyroid function in the nutritionally obese child and adolescent. *Current opinion pediatr* 2011; 23(4): 415-20.
9. Grandone A, Santoro N, Coppola F, et al. Thyroid function derangement and childhood obesity: an Italian experience. *BMC endocrine dis* 2010; 10(8): 1-7.
10. Ozer S, Bütün İ, Sönmezgöz E, et al. Relationships among thyroid hormones and obesity severity, metabolic syndrome and its components in Turkish children with obesity. *Nutr Hosp* 2015; 32(2): 645-51.
11. Reinehr T. Obesity and thyroid function. *Mol Cell Endocrinol* 2010; 316(2): 165-71.
12. Cerbone M, Capalbo D, Wasniewska M, et al. Cardiovascular risk factors in children with long-standing untreated idiopathic subclinical hypothyroidism. *J Clin Endocrinol Metab* 2014; 99(8): 2697-703.
13. World Health Organization. Training Course on Child Growth Assessment, WHO Child Growth Standards. 2008. Available from: http://www.who.int/childgrowth/training/module_h_dir_ectors_guide.pdf.
14. Blössner M SA, Borghi E, Onyango A, Onis Md. WHO AnthroPlus for Personal Computers Department of Nutrition for Health and Development, Geneva, Switzerland 2009. Available from: <http://who-anthroplus.software.informer.com/download/>.
15. Zurakowski D, Di Canzio J, Majzoub JA. Pediatric reference intervals for serum thyroxine, triiodothyronine, thyrotropin, and free thyroxine. *Clin Chem* 1999; 45(7): 1087-91.
16. Ghergherehchi R, Hazhir N. Thyroid hormonal status among children with obesity. *Therap Advanc Endocrinol Met* 2015; 6(2): 51-5.
17. Dahl M, Ohrt JD, Fonvig CE, et al. Subclinical hypothyroidism in danish lean and obese children and

- adolescents. *J Clin Res Pediatr Endocrinol* 2017; 9(1): 8-16.
18. Bougle D, Morello R, Brouard J. Thyroid function and metabolic risk factors in obese youth, changes during follow-up: a preventive mechanism? *Exp Clin Endocrinol Diab* 2014; 122(9): 548-52.
19. Mansour M, Nassef YE, Shady MA, et al. Metabolic syndrome and cardiovascular risk factors in obese adolescent. *Macedonian J Med Sci* 2016; 4(1): 118-21.
20. Witte T, Ittermann T, Thamm M, et al. Association between serum thyroid-stimulating hormone levels and serum lipids in children and adolescents: a population-based study of german youth. *J Clin Endocrinol Metab* 2015; 100(5): 2090-7.
21. Lundbäck V, Ekblom K, Hagman E, et al. Thyroid-stimulating hormone, degree of obesity, and metabolic risk markers in a cohort of obese Swedish children. *Horm Res Paediatr* 2017; 88(2): 140-6.
22. Minami Y, Takaya R, Takitani K, et al. Association of thyroid hormones with obesity and metabolic syndrome in Japanese children. *J Clin Biochem Nutr* 2015; 57(2): 121-8.
23. García-García E, Vázquez-López MA, García-Fuentes E, et al. Thyroid function and thyroid autoimmunity in relation to weight status and cardiovascular risk factors in children and adolescents: A population-based study. *J Clin Res Pediatr Endocrinol* 2016; 8(2): 157-62.
24. Reinehr T, de Sousa G, Andler W. Hyperthyrotropinemia in obese children is reversible after weight loss and is not related to lipids. *J Clin Endocrinol Metab* 2006; 91(8): 3088-91.
25. Pacifico L, Anania C, Ferraro F, et al. Thyroid function in childhood obesity and metabolic comorbidity. *Clinica Chimica Acta* 2012; 413(3): 396-405.
26. De Pergola G, Ciampolillo A, Paolotti S, et al. Free triiodothyronine and thyroid stimulating hormone are directly associated with waist circumference, independently of insulin resistance, metabolic parameters and blood pressure in overweight and obese women. *Clin Endocrinol* 2007; 67(2): 265-9.
27. Lee CMY, Huxley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol* 2008; 61(7): 646-53.
28. Nathan BM, Moran A. Metabolic complications of obesity in childhood and adolescence: more than just diabetes. *Cur Opin Endocrinol Diabet Obes* 2008; 15(1): 21-9.