DOI: 10.4274/tpa.46.05

Mildly elevated TSH levels in obese children: What kind of problem is this?

R. Gül Yeşiltepe Mutlu, Elif Özsu, Filiz Mine Çizmecioğlu, Şükrü Hatun

Kocaeli University Medical Faculty, Division of Pediatric Endocrinology and Diabetes, Kocaeli, Turkey

Summary

Aim: To determine the effects of obesity on thyroid functions in children.

Material and Method: The records of 132 patients who were followed up in our pediatric endocrinology and diabetes department with the diagnosis of obesity from March 2006 to May 2009 were investigated retrospectively. Anthropometric measurements, serum lipid profiles, thyroid hormone levels, fasting blood glucose and insulin levels were evaluated. TSH levels of the patients whose HOMA-IR (homeostasis model assessment of insulin resistance) values were <3.16 and >3.16 were compared. Correlation between TSH levels and HOMA-IR levels and BMI (Body mass index) was investigated.

Results: TSH levels of seventeen patients (12.9%) were above the 97.5th persentile and TSH levels of fifty-one patients (38.7%) were above the 90th persentile. None of the patients whose TSH levels were above the 97.5th persentile had low free/ total T4 levels. There was no significant difference in the TSH levels when the patients whith HOMA-IR <3.16 and HOMA-IR >3.16 were compared. There was an insignificant, positive, weak correlation between TSH levels and HOMA-IR and BMI.

Conclusions: TSH levels in obese children may be elevated without any change in peripheral thyroid hormone levels. This situation should not be evaluated as hypothyroidism and L- thyroxine treatment should not be started on the first evaluation. *(Turk Arch Ped 2011; 46: 33-6)*

Key words: Body mass index, HOMA-IR, obesity, TSH

Introduction

In recent years, obesity has become an important health problem threatening public health. It is known that obesity affects endocrine functions and its effects on thyroid functions in children and adolescents and their clinical implications are emphasized. In many studies, serum TSH levels have been shown to be higher in obese adults, adolescents and children compared to individuals without obesity, but no reduction in free and total T4 level accompanied this state (1-6). In this study, it was aimed to investigate the effects of obesity on thyroid hormones in children and the relation of these effects with the degree of obesity and insulin resistance.

Material and Method

One hundred thirty two patients who were followed up in the Division of Pediatric Endocrinology and Diabetes in Kocaeli University Medical Faculty with the diagnosis of obesity from March 2006 to May 2009 and whose thyroid functions were evaluated were investigated retrospectively. A Body Mass Index (BMI) higher than the 95th percentile was considered as obesity. BMI percentiles were assessed according to the study performed by Bundak et al (7) in 2006 for children with an age of 6 years and older and according to CDC (centers of disease control and prevention) data of 2000 for children older than 6 years (8). Subjects with known history of thyroid disease were excluded from the study.

Address for Correspondence: R. Gül Yeşiltepe Mutlu MD, Kocaeli University Medical Faculty, Division of Pediatric Endocrinology and Diabetes, Kocaeli, Turkey
E-mail: gulyesiltepe@yahoo.com **Received:** 08.03.2010 **Accepted:** 12.07.2010

Antropometric measurements, serum TSH, free T4 and/or total T4 level, serum lipid levels, thyroid hormone levels, fasting blood glucose and insulin levels were recorded and HOMA-IR value was calculated (fasting insulin x fasting blood glucose (mmol/L)/22.5). Thyroid hormone levels were assessed according to the range in the age-appropriate source (9). Treshold value for HOMA-IR was considered to be >3.16 and subjects with a value higher than this were classified as subjects with positive insulin resistance (10). Thyroid functions in the study group were compared in the subjects with positive insulin resistance and negative insulin resistance and by the degree of obesity. Data were analysed on SPSS 13.0 Statistical Program. Comparisons for independent groups were done with chi-square test and correlation analysis was done with Pearson method. A p value of <0.05 was considered statistically significant.

Results

Eigthy three (62.9%) of 132 subjects recruited to the study were female and 49 (37.1%) were male. Mean age was 11.9±3.18 years (5.1-17.9). 24% of the subjects (n:32) were in the preadolescence period, 33% (n:44) were in the middle of adolescence and 43% (n:56) had completed adolescence. Mean BMI (Body Mass Index) value was 30.61 ±4.65 (21.7-42) and mean BMI Standard deviation score (SDS) was found to be 2.79±0.62 (2-5.7). Acanthosis nigricans was present in 76 of the subjects (57.6%). HOMA-IR was >3.16 in 50% of the subjects and <3.16 in 50% of the subjects. Mean HOMA-IR value was 1.9±1.02 in the subjects in the preadolescence period, 3.07±1.7 in the subjects in the adolescence period and 5.69±8.7 in the subjects who had completed adolescence. Mean serum insulin level was found to be 16±10.57 (1.0-69) mU/mL. Mean TSH level of the subjects was found to be 3.42±1.57 mU/mL (0.77-9.0). TSH level was between the 90th and 97.5th percentile according to age in 34 subjects (25,8%) and above the 97.5th percentile in 17 subjects (12,9%). In a total of 51 subjects (38.7%), TSH level was found to be above the 90th percentile. Thyroid autoantibodies were found to be negative in the subjects with TSH level above the 90th percentile. Free T4 (fT4) level was evaluated in 116 subjects and was found to be between the 10th and 97.5th percentile in 109 (94%) and above the 97.5th percentile in 7 (6%). Mean free T4 was found to be 16.84±4.2 pmol/L. fT4 level was not below normal in any subject in the group with a TSH level above the 97.5th percentile. fT4 levels in the subjects with TSH level above the 97.5th percentile are shown in Table 1. Total T4 level was evaluated in 52 subjects and the mean value was found to be 9.27±1.89 mg/mL (6.15-14.50). Mean serum cholesterol level was found to be 165.1±33.9 mg/dl and mean triglyceride level was found to be 111.1±53.7 mg/dl. Mean HDL cholesterol level was 44.5±9.3 mg/dl and mean LDL cholesterol level was 99±27.4 mg/dl. Anthropometric parameters and laboratory findings of the subjects are shown in Table 2. The subjects were divided into two groups; one group with a HOMA-IR value higher than 3.16 (group 1, n:66) and the other group with a HOMA-IR value lower than 3.16 (group 2, n:50). When TSH levels of these two groups were compared, no statistically significant difference was found (p=0.697) (Table 3). When the subjects were divided into two groups according to BMI SDS values with one group with a BMI SDS value between 2 and 3 (n:85) and the other group with a BMI SDS value of >3 (n:46), no statistically significant difference was found in terms of TSH levels (p<0.05) (Table 4). There was an insignificant, positive, weak correlation between TSH levels and HOMA-IR and BMI (Table 5).

Discussion

In recent years, many studies about the effects of obesity on thyroid functions have been conducted and serum TSH levels have been shown to be mildly higher in obese children, adolescents and adults compared to individuals without obesity (1-5). It is known that no change in free or total T4 levels accompany this mild increase in TSH level (3, 5, 6). High TSH levels were found in 7.5% of 290 obese children in the study performed by Stichel et al. (11) and in 10.8% of 185 obese children in the study performed by Bassem et al. (12). Similarly, THS level was found to be above the 97.5th percentile in 13% (n:17) of 132 subjects included in the study group in our study and this rate is close to the rates reported in the literature. It has been shown that increase in peripher-

Table 1. Free T4 levels in the subjects with TSH level above the 97.5th percentile

Subject	TSH level (mU/mL)	fT4 level (pmol/L)
1	6.17	16.8
2	5.78	15.3
3	5.84	16.3
4	5.89	16.3
5	7	16.7
6	6.16	14.3
7	7.1	17.1
8	7.23	15.8
9	6.82	16.8
10	6.75	20.2
11	5.9	14.8
12	6.55	13.8
13	7.43	13.8
14	7.31	21.9
15	9	11.2
16	4.75	16.5
17	4.92	14.8

al thyroid hormones may be present along with high TSH levels in obese children. The cause of this is not completely known, but it is thought that it might be caused by thyroid hormone resistance similar to insulin resistance (13). In our study, however, fT4 levels were found to be normal in the subjects with high levels of TSH.

Although the effect of obesity on TSH has not been fully elucidated yet, it has been shown that this is not related to iodine deficiency or autoimmune thyroiditis (5,6,11,13). The fact that evidence of autoimmune throiditis was not found in any of the subjects with high TSH level supports literature information (5,6,11,13). In our country, iodine protection is being performed since 1998 by use of iodized salt and a marked decrease in iodine deficiency has been achieved, but still the prevalence of moderate-severe iodine deficiency was reported to be 27.8% in a publication reporting the current iodine status (14). Since our study was performed retrospectively, urine iodine levels were not assessed in the subjects. This may be evaluated as a weak point in our study.

In the studies performed recently, it has been suggested that adipose cells contain numerous TSH receptors and this explains the relation between obesity and TSH (15). It is known that TSH production is regulated by some neurotransmitters (neuropeptide-Y, melanocyte-stimulating hormone, agouti-related peptide) which regulate body weight and satiety. In addition, some studies have shown a positive correlation between leptin level and TSH (16-18).

Some studies have shown a positive correlation between body mass index and TSH level (2,19). However, 20 overweight children were compared to 30 obese children in terms of TSH level in the study performed by Kumar et al. (20) published in 2009 and no statistically significant difference was found between the two groups. Again in the same study, no relation was found between TSH level and BMI (20). In our study, no statistically significant difference was found in TSH levels between the groups with a BMI SDS value of 2-3 and >3 and no statistically significant correlation was found between TSH level and BMI.

Some studies have shown a strong correlation between TSH level and insulin resistance and BMI in obese individuals (20,21). In our study, however, no statistically significant correlation was shown between HOMA-IR and TSH level.

In a study comparing TSH levels before and after weight reduction, the finding that no significant decrease in TSH levels occured after weight reduction suggested that the cause of obesity in these patients was a neuroendocrine dysfunction leading to bioinactive TSH release (13). However, the same investigator compared TSH levels before and after weight reduction in 240 obese children and found that there was a significant decrease in TSH level with weight reduction and emphasized that high TSH level was a result of obesity rather that a cause based on these findings (5). Eliakim et al.(22) showed that thyroxine treatment had no positive effect in children with high TSH.

Table 2. Anthropometric parameters and laboratory findings of the subjects

	Mean	SD	Range
Age (years)	11.9 years	3.18	5.1-17.9
BMI (kg/m^2)	30.60	4.71	20.6 - 42
Insulin (ıu/mL)	16	10.57	1.0 - 69
HOMA-IR	3.9	5.97	0.2 -12.9
TSH (mıu/L)	3.42	1.57	0.77-9.0
fT4 (pmol/L)	16.84	4.2	11-48.6
Total cholesterol (mg/dL)	165.1	33.9	64-246
HDL cholesterol (mg/dL)	44.5	9.3	22-111
LDL cholesterol (mg/dL)	99	27.4	9-172.6
Triglyceride (mg/dL)	111.1	53.7	24-338
	n	%	
Gender (female/male)	83/49	62.9 / 37.1	
Presence of acanthosis nigricans	76	57.6	
Subjects with HOMA-IR>3.16	66	50	
Subjects with TSH>97.5 P	17	12.9	
Subjects with TSH>90 P	51	38.7	
Subjects with TSH between the 90th and 97.5th P	34	25.8	

Table 3. Comparison of TSH levels according to HOMA-IR values

	HOMA-IR<3.16 (n:66)		HOMA-IR>3.16 (n:66)		p
	n	%	n	%	
Subjects with TSH 90-97.5 P	15	22.7	19	28.7	>0.05
Subjects with TSH>97.5 P	8	12.1	9	13.6	>0.05

Table 4. Comparison of TSH levels according to BMI-SDS values

	Subjects with BMI SDS: 2-3 (n: 85)		Subjects with BMI SDS> 3 (n: 46)		P
	n	%	n	%	
Subjects with TSH 90-97,5 P	19	22.3	15	32.6	>0.05
Subjects with TSH>97.5 P	11	12.9	6	13	>0.05

BMI: Body Mass Index
SDS: Standard Deviation Score

Table 5. Correlation of TSH with BMI and HOMA-IR values

	TSH r	p
BMI	0.01	0.91
HOMA-IR	0.026	0.79

BMI: Body Mass Index

Conclusively, thyroid functions should be interpreted meticulously, peripheral thyroid hormones should be measured (especially T4) and acquired hypothyroidism should be excluded in obese children. In subjects with normal T4 levels and mildly increased TSH level, it should be kept in mind that this is a result of obesity, rather than a cause and starting treatment on the first evaluation should be avoided.

Conflict of interest: None declared

References

1. Nyrnes A, Jorde R, Sundsfjord J. Serum TSH is positively associated with BMI. Int J Obes (Lond) 2006; 30: 100-5. (Abstract) / (Full Text)
2. Knudsen N, Laurberg P, Rasmussen LB, et al. Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. Clin Endocrinol Metab 2005; 90: 4019-24. (Abstract) / (Full Text) / (PDF)
3. Moulin de Moraes CM, Mancini MC, de Melo ME, et al. Prevalence of subclinical hypothyroidism in a morbidly obese population and improvement after weight loss induced by Roux-en-Y gastric bypass. Obes Surg 2005; 15: 1287-91. (Abstract) / (PDF)
4. Iacobellis G, Ribaudo MC, Zappaterreno A, Iannucci CV, Leonetti F. Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. Clin Endocrinol (Oxf) 2005; 62: 487-91. (Abstract) / (PDF)
5. 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: 3088-91. (Abstract) / (Full Text) / (PDF)
6. Reinehr T, Isa A, de Sousa G, Dieffenbach R, Andler W. Thyroid hormones and their relation to weight status. Horm Res 2008;70: 51-7. (Abstract) / (Full Text) / (PDF)
7. Bundak R, Furman A, Gunoz H, Darendeliler F, Bas F, Neyzi O. Body mass index references for Turkish children. Acta Pediatr 2006: 95; 194-8. (Abstract)
8. Centers for disease control and prevention. http://www.cdc.gov/growthcharts/p://www.cdc.gov/growthcharts/clinical_charts.htm#
9. Kapelari K, Kirchlechner C, Högler W, Schweitzer K, Virgolini I, Moncayo R. Pediatric reference intervals for thyroid hormone levels from birth to adulthood: a retrospective study. BMC Endocr Disord 2008; 27: 8-15. (Abstract) / (Full Text) / (PDF)
10. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics 2005; 115: 500-3. (Abstract) / (Full Text) / (PDF)
11. Stichel H, l'Allemand D, Grüters A. Thyroid function and obesity in children and adolescents. Horm Res 2000; 54: 14-9. (Abstract) / (Full Text) / (PDF)
12. Dekelbab BH, Abou Ouf HA, Jain I. Prevalence of elevated thyroid-stimulating hormone levels in obese children and adolescents. Endocr Pract 2010;16:187-90. (Abstract) / (PDF)
13. Reinehr T, Andler W. Thyroid hormones before and after weight loss in obesity. Arch Dis Child 2002; 87: 320-3. (Abstract) / (Full Text) / (PDF)
14. Erdoğan MF, Ağbaht K, Altunsu T, et al. Current iodine status in Turkey. J Endocrinol Invest 2009; 32: 617-22. (Abstract)
15. Reinehr T. Obesity and thyroid function. Mol Cell Endocrinol 2010; 316: 165-71. (Abstract) / (PDF)
16. Rohner-Jeanrenaud F, Jeanrenaud B. The discovery of leptin and its impact in the understanding of obesity. Euro J Endocrinol 1996; 135: 649-50. (Abstract) / (PDF)
17. Légrádi G, Emerson CH, Ahima RS, Flier JS, Lechan RM. Leptin prevents fasting-induced supression of prothyrotropin-releasing hormone messenger ribonucleic acid in neurons of the hypothalamic paraventricular nucleus. Endocrinology 1997;138: 2569-76. (Abstract) / (Full Text) / (PDF)
18. Kim MS, Small CJ, Stanley SA, et al. The central melanocortin system affects the hypothalamo-pituitary thyroid axis and may mediate the effect of leptin. J Clin Invest 2000; 105: 1005-11. (Abstract) / (PDF)
19. Bastemir M, Akin F, Alkis E, Kaptanoglu B. Obesity is associated with increased serum TSH level, independent of thyroid function. Swiss Med Wkly 2007; 137: 431-4. (Abstract) / (PDF)
20. Hari Kumar KV, Verma A, Muthukrishnan J, Modi KD. Obesity and thyrotropinemia. Indian J Pediatr 2009; 76: 933-5. (Abstract) / (PDF)
21. Galofré JC, Pujante P, Abreu C, et al. Relationship between thyroid-stimulating hormone and insulin in euthyroid obese men. Ann Nutr Metab 2008; 53: 188- 94. (Abstract) / (Full Text) / (PDF)
22. Eliakim A, Barzilai M, Wolach B, Nemet D. Should we treat elevated thyroid stimulating hormone levels in obese children and adolescents ? Int J Pediatr Obes 2006; 1: 217-21. (Abstract)