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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 10 (6): 905-909, 2007
ISSN 1028-8880

Body Mass Index and Thyroid Function in Adolescent Girls

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Abstract: The present research was conduted to examine the relationship between thyroid function and body mass index. A cross-sectional study was carried out in Lar province and its' vicinity in south of Iran. By stepwise random sampling from all public girls' high schools, 227 high school participants (aged 12-21) were selected. Serum samples were collected and assayed for Triiodothyronine (T3), thyroxine (T4), thyroid stimulating hormone (TSH), reverse triiodothyronine (rT3), free thyroxine (FT4), free triiodothyronine (FT3). Weight and height were measured and body mass index (BMI) were calculated (weight (kg)/height^2 (m)). Subgroup analysis was done according to body mass index. TSH, T4 and rT3 were correlated with BMI ($r = 0.66$, $p = 0.001$ and $r = 0.12$, $p = 0.05$ and $r = 0.65$, $p = 0.001$, respectively). Adolescent girls with BMI ≥ 25 kg m^{-2} showed higher serum TSH, T4 and rT 3 than subjects with BMI < 25 kg m^{-2} ($p = 0.001$, $p = 0.05$ and $p = 0.001$, respectively). Present results showed that, although thyroid function was normal in the studied participants TSH and rT3 were positively correlated to BMI. TSH and rT3 could present a marker of altered energy balance in overweight and obese adolescent girls.

Key words: Body mass index, thyroid, adolescent, girls

INTRODUCTION

Maintenance of weight gain or loss is associated with compensatory changes in energy expenditure that oppose the maintenance of a body weight that is different from the usual weight (Leibel *et al*., 1995). Weight gain results when energy intake exceeds energy expenditure and even a modest, but sustained, reduction in energy dissipation is a predisposing factor for the disorder. Thyroid hormones (tri-iodothyronine, T3 and its precursor thyroxine, T4) play an important role in development and physiology of vertebrate organisms and altered T3/T4 levels manifest themselves in energy metabolism and body growth (Forrest, 1994; Freake and Oppenheimer, 1995).

Thyroid hormones have been indicated to have at least a permissive role in adaptive thermogenesis by influencing several aspects of energy metabolism, such as substrate cycling, ion cycling and mitochondrial proton leaks (Wu *et al*., 2000). Whether a deficit in resting energy expenditure plays a role in the development of weight gain leading to obesity is matter of debate (Goran, 2000).

With respect to thyroid function, there are conflicting results in the literature with higher, lower or similar thyroid hormone levels in obese compared with normal weight subjects (Chomard *et al*., 1985; Duntas *et al*., 1991; Naslund *et al*., 2000). Some studies have focused on the relationship between leptin and energy expenditure as well as thyroid function. Leptin physiologically increases energy expenditure (Niskanen *et al*., 1997), but in obesity the situation is less clear due to the condition of leptin resistance of most obese patients (Lonnqvist *et al*., 1999). As far as thyroid function is concerned, hypothyroid patients have been reported to have higher levels of leptin than healthy subjects matched for body mass index (Leonhardt *et al*., 1998), but other studies have not confirmed this finding (Sesmilo *et al*., 1998; Diekman *et al*., 1998). Experiments on animals have shown a correlation between thyroid hormones and changes in weight (Koristschoner *et al*., 2001).

The possible implications of these slight differences in thyroid function for the risk of gaining weight and developing overweight or obesity have high actually with the present worldwide epidemic of obesity and complications associated with obesity. Overweight and obesity are now considered as a serious health problem, with an increasing prevalence worldwide (Allison *et al*., 1996). Life style is undoubtedly of major importance for weight gain in the population, but interaction with other factors is far from elucidated in detail. Therefore, in order to evaluate a possible association between thyroid hormone levels and body mass index, we conducted a cross-sectional population based study in adolescent Iranian girls.

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MATERIALS AND METHODS

Participants: A cross-sectional study was carried out in Lar province and its' vicinity in southern Islamic Republic of Iran. By stepwise random sampling from grades 1 to 4 high-school girls 227 participants (aged 12 to 21 years old) were selected. Participants with a history of thyroid disease or with endocrine or metabolic disorders and who were taking thyroid hormones or iodine-containing drugs were excluded. Participants were given an oral and a written explanation of the study.

Demographic data, menstruation, any concurrent illness history, medication and vitamin and mineral supplementation were collected by interviews and anthropometric indices were determined for each participant. Anthropometric assessments included measurement of weight and height. Body weight was measured to the nearest 0.1 kg using the Seca 713 scale while subjects were minimally clothed. Height was determined using measuring tape without shoes and subsequently body mass index was calculated by dividing weight (kg) by squared height (m^2).

Biochemical analyses: Ten milliliter fasting venous blood samples were drawn from the arm for determination of total and free thyroxine, total and free triiodothyronine, thyrotropin, T3RU and reverse triiodothyronine. Serum tT4, tT3, TSH, fT4, fT3, T3RU and rT3 were determined by radioimmunoassay (Henry 1996), using commercially available kits (Belgium ZenTech for rT3 and American DSL for the rest).

Normal values for thyroid hormone indices, as indicated by the manufacturers of the assay kits, were as follows: TSH (mIU mL^{-1}): 0.5-5.1, tT4 (μg dL^{-1}): 3.4-13.6, fT4 (pg mL^{-1}): 8.0-20.0, tT3 (ng dL^{-1}): 61-219, fT3 (pg mL^{-1}): 1.5-5.0, rT3 (ng dL^{-1}): 20-50 and T3RU (%): 30-40.

Statistical analyses: Statistical analyses were performed by SPSS statistical software (11.0 version, SPSS Inc., Chicago, 2001). Data are expressed as mean and standard deviation (SD). Statistical significant differences were test by the Student t-test. We used linear regression analysis to illustrate possible interrelationships among thyroid hormones and body mass index. The stepwise logistic regression method was performed to determine the most significant predictors of changes in body mass index. A $p<0.05$ was considered significant in all statistical tests.

Ethical aspects: The study protocol was reviewed and approved by the Human Ethics Committee of Research Council of the Dean of Research Affair of Tehran University of Medical Sciences and participants' parents or guardian were asked to read and sign an informed consent document.

RESULTS

A total of 227 adolescent girls selected for participation in this study. As shown, BMI of our study group ranged from 17.75 to 31.24 kg m^{-2}. Thyroid indices shown (Table 1) that normal thyroid function, as defined by normal levels of thyroid functions was preserved in our participants. In order to compare biochemical characteristics of normal-weight participants with over-weight or obese participants, we categorized all participants in two groups, those with BMI between 18.5

Table 1: Anthropometric and biochemical characteristics of selected subjects*

Range	Mean±SD	Indice
Age (year)	16.13±1.82	12.00-21.00
Weight (kg)	56.54±5.70	42.00-70.00
BMI (kg m^{-2})	23.86±2.7	17.75-31.24
TSH (μU mL^{-1})	2.36±0.42	1.40-3.60
T4 (μg dL^{-1})	8.73±0.73	7.00-10.60
FT4 (pg dL^{-1})	10.66±1.37	8.00-15.00
T3 (ng dL^{-1})	133.50±16.88	110.00-177.00
FT3 (pg mL^{-1})	2.71±0.40	1.60-3.70
rT3 (ng dL^{-1})	35.50±8.20	18.00-51.00
T3RU (%)	27.37±3.35	20.60-27.37
T3/T4 ratio	15.40±2.40	11.50-23.40

* n = 227

Table 2: Demographic parameters of normal-weight and abnormal-weight participants

Range	Normal-weight* (BMI = 18.5-249)	Over-weight** (BMI ≥ 25)	p-value
Age (year)	15.85±1.70	16.70±2.00	<0.1
Weight (kg)	54.23±4.80	61.60±4.10	<0.001
BMI (kg m^{-2})	22.43±1.80	27.00±1.50	<0.001
TSH (μU mL^{-1})	2.20±0.36	2.70±0.35	<0.001
T4 (μg dL^{-1})	8.70±0.75	8.97±0.65	<0.05
FT4 (pg dL^{-1})	10.70±1.40	10.40±1.20	<0.1
T3 (ng dL^{-1})	132.60±16.70	135.68±17.60	<0.2
FT3 (pg dL^{-1})	2.70±0.40	2.70±0.40	<0.7
rT3 (ng dL^{-1})	32.00±6.70	42.90±5.60	<0.001
T3RU (%)	27.40±3.40	27.30±3.30	<0.8
T3/T4 ratio	15.39±2.30	15.40±2.50	<0.9

* n = 154, ** n = 69

Table 3: Correlation between BMI and thyroid hormone concentrations in selected participants

Range	r*	r^2	β	p-value
Age	0.33	0.11	0.49	<0.001
TSH	0.66	0.44	0.43	<0.001
TT4	0.12	0.01	0.45	<0.05
FT4	0.10	0.01	0.20	<0.1
TT3	0.11	0.01	0.01	<0.09
FT3	0.02	0.001	0.18	<0.7
rT3	0.65	0.42	0.21	<0.001
T3UP	0.02	0.001	0.02	<0.7
T3/T4	0.02	0.001	0.02	<0.7

*n = 227

to 24.9 as normal-weight and those greater than 25 as abnormal-weight. Table 2 shows the result of comparison of biochemical characteristic between two groups. Sixty nine participants had a BMI≥25 kg m^{-2} and 154 participants showed a BMI<25 kg m^{-2}. No differences on age between two groups were found. Participants with BMI≥25 kg m^{-2} showed higher serum TSH and rT3 than normal-weight participants, 2.70±0.35 vs. 2.2±0.36 mU L^{-1} ($p<0.001$) and 42.9±5.6 vs. 32.0±6.7 ng dL^{-1} ($p<0.001$), respectively. We have not observed significant difference in tT4, tT3, FT4, FT3, T3/T4 ratio and T3 RU in two groups.

Pearson correlation coefficients between BMI and the indices of thyroid hormone in all participants before group assignment are shown in Table 3. As Table 3 shows, some of thyroid indices significantly correlated with BMI. Further investigation into the changes in BMI in these participants, was carried out using multiple regression analysis in which the independent variables included were: TSH, tT4, tT3, fT4, fT3, rT3 T3RU, T3/T4 ratio. Using stepwise regression procedure, only TSH, rT3 and T4 contributed significantly to the $r^2 = 0.61$, $p<0.001$).

DISCUSSION

Body mass index is not static and varies throughout life in response to physical activity and nutritional, social and psychologic factors and also correlates well with the concentrations of several blood components: insulin (Begdade *et al*., 1967), glucose (Munan *et al*., 1978), triglycerides (Lellouch *et al*., 1973), high-density lipoprotein cholesterol (Glueck *et al*., 1980) and ureate (Begdade *et al*., 1967). Also, concentrations of hormones not primarily involved in energy metabolism may vary with body mass or body composition, e.g., estrogens in obese postmenopausal women (Judd *et al*., 1980).

The interrelationship between obesity and thyroid physiology have been studied both in the etiology of obesity and as a reason for using thyroid hormones in weight loss regimens. There are conflicting data in the literature regarding the relationship between obesity and thyroid hormones. Most studies have reported normal serum thyroid hormone levels, including total and free T4 and T3 as well as reverse T3 (rT3) (Lacobellis *et al*., 2005; Rosenbaum *et al*., 2000; Sari *et al*., 2003). However, some studies have reported elevated T3 and TSH levels among obese patients (Knudsen *et al*., 2005; Roti *et al*., 2002; Krotkiewski, 2000).

Our results showed that the concentrations of some thyroid hormones i.e, total T4, TSH and rT3 but not total T3, free T4 and free T3 are dependent upon body mass index. The differences in the concentration of total T4 and thyrotropin between participants with normal body mass index and high BMI are small, but may be clinically significant.

Moderate rise in total T4 concentrations of our participants with BMI higher than 25, has been shown in a number of other studies (Kiortis *et al*., 1999). Knudsen *et al*. (2005) found a possible association between BMI and category of serum TSH (Knudsen *et al*., 2005). As Knudsen noted, it could be speculated that the association between serum TSH and body mass index in the present study is caused by signals from adipose tissue. Leptin produced by adipocytes has important influences on central regulation of thyroid function through stimulation of TRH. This seems to be important for down-regulation of thyroid function in states of energy deficits, but the importance for modulation of thyroid function under more physiological conditions is uncertain (Chan *et al*., 2003; Zimmermann *et al*., 2003). A positive correlation has been found between serum leptin and serum TSH in several studies (Zimmermann *et al*., 2003), which corresponds to the positive association between BMI and TSH found in our study and Knudsen study. Studies of subjects undergoing heavy weight reduction do not show homogenous results, however weight reduction has been found associated with reduction in both serum TSH and T3 levels (Papavramidis *et al*., 1995; Matzen and Kventy, 1989), reduction in serum TSH levels alone (Sari *et al*., 2003; Yashkov *et al*., 2000), reduction in T3 level alone (Rosenbaum *et al*., 2000), or no change in thyroid function test (Naslund *et al*., 2000). The cause of the increased thyroid hormone concentrations in obesity is unclear. Increased thyroid hormone concentrations could point to hormone resistance, similar to insulin resistance in obesity. In support of this theory is the fact that in obesity T3 receptors are decreased (Burman *et al*., 1980) and the negative feedback between TSH and the peripheral thyroid hormones (T3, T4) is decreased, as both TSH and the peripheral thyroid hormones are increased in obesity.

Although this study could not revealed a significant difference in T3 concentration between two groups, but our findings support the hypothesis that an increase in rT3 is related to changes in BMI. Presumably, overweight subjects tend to metabolize thyroid hormones via a deactivating pathway, so, a small fraction of T4 is converted to T3 and a larger proportion is metabolized to a physiologically inactive metabolite, rT3. rT3 may decrease oxygen consumption, inhibit conversion of T4 to T3 and inhibit cathecholamine mediated lipolysis, effects that are the opposite of T3 (Chopra, 1981).

However the potency of rT3 *in vitro* to inhibit thyroliberin-induced release of thyrotropin is low. Therefore, the positive correlation with BMI in our study may reflect a correlation of serum concentrations of rT3 with T4 concentrations in health.

In summary, synthesis of thyroid hormones is regulated by several factors, among which energy intake is a minor one (Katzeff and Selgrad, 1991). The effects of changes in body weight on thyroid function are controversial, probably due to different study design (human or animal), subject population, iodine status and treatment modalities (diet, exercise, drug,...).

Differences in concentrations of thyroid hormones (TSH, tT4, rT3) concomitant with differences in body mass index observed in this study could perhaps be secondary to longstanding minor alterations in energy expenditure, differences in food consumptions-calorie intake, consumption of food, food iodine content and fasting-refeeding having been reported to influence thyroid hormone content. There is still a need for further research into the cause of the changes in thyroid hormones in overweight and obesity.

ACKNOWLEDGMENTS

The authors are indebted to the Dean of Research Affairs of Tehran University of Medical Sciences for financial support and the participating students, their mothers and teachers, for their compliance and patience.

REFERENCES

Allison, D.B., K.R. Fontaine, J.E. Manson, J. Stevens and T.B. VanItallie, 1999. Annual deaths attributable to obesity in the US. JAMA., 282: 1530-1538.

Begdade, J.D., E.L. Bierman and D. Porte, 1967. The significance of basal insulin levels in the evaluation of the insulin response to glucose in diebetic and nondiabetic subjects. J. Clin. Invest., 46: 1549-1557.

Burman, K.D., K.R. Latham and Y.Y. Djuh *et al*., 1980. Solubilized nuclear thyroid hormone receptors in circulating human mononuclear cells. J. Clin. Endocrinol. Metab., 51: 106-116.

Chan, J.L., K. Heist, A.M. DePaoli, J.D. Veldhuis and C.S. Mantzoros, 2003. The role of falling leptin levels in the neuroendocrine and metabolic adaptation to short term starvation in healthy men. J. Clin. Invest., 11: 1409-1421.

Chomard, P., G. Vernhes, N. Autissier and G. Debry, 1985. Serum concentration of total T4, T3, reverse T3 and free T4, T3 in moderately obese patients. Human Nutr. Clin. Nut., 39: 371-378.

Chopra, I.J., 1981. Triiodothyronines in health and disease. Springer-verlag, Berlin, hormones metabolism during over nutrition. J. Clin. Investigation, 64: 1336-1347.

Diekman, M.J., J.A. Romijn, E. Endert, H. Sauerwein and W.M. Wiersinga, 1998. Thyroid hormones modulate serum leptin levels: Observations in thyrotoxic and hypothyroid women. Thyroid, 1081-1086.

Duntas, L., H. Hauner, J. Rosenthal and E.F. Pfeiffer, 1991. Thyrotropin releasing hormone (TRH) immunoreactivity and thyroid function in obesity. Int. J. Obesity, 15: 83-87.

Forrest, D., 1994. The erb/Athyroid hormone receptor genes in development of the central nervous system. Semin Cancer Biol., 5: 167-176.

Freake, H.C. and J.H. Oppenheimer, 1995. Thermogenesis and thyroid function. Annu. Rev. Nutr., 15: 263-291.

Glueck, C.J., H.J. Taylor and D. Jacobs *et al*., 1980. Plasma high density lipoprotein cholesterol: Association with measurements of body mass. Circulation, 62 (Suppl IV): 62-69.

Goran, M.I., 2000. Energy metabolism and obesity. Med. Clin. North. Am., 84: 347-362.

Henry, J.B., 1996. Methods of Clinical Laboratory Management and Diagnosis. W.B. Saunders, pp: 89-112.

Judd, H.L., B.J. Davidson and A.M. Frumar *et al*., 1980. Serum androgens and estrogens in postmenopausal women with and without endometrial cancer. Am. J. Obstet Gynecol., 136: 859-871.

Katzeff, H.L. and C. Selgrad, 1991. Maintenance of thyroid hormone production during exercise-induced weight loss. Am. J. Physiol., 261: E382-E388.

Kiortis, D.N., I. Durack and G. Turpin, 1999. Effects of a low-calorie diet on resting metabolic rate and serum triiodothyronine levels in obese children. Eur. J. Pediatr., 158: 446-450.

Knudsen, N., P. Laurberg, L.B. Rasmussen, I. Bulow, H. Perrild, L. Ovesen and T. Jorgensen, 2005. Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. J. Clin. Endocr. Metab., 90: 4019-4024.

Koritschoner, N.P., M. Alvarez-Dolado and S.M. Kurz *et al*., 2001. Thyroid hormone regulates the obesity gene tub. EMBO Rep., 2: 499-504.

Krotkiewski, M., 2000. Thyroid hormones and treatment of obesity. Int. J. Obesity and Related Meta. Disorders, 63: 135-139.

Lacobellis, G., M.C. Ribaudo, A. Zappaaterreno, C.V. Lannucci and F. Leonetti, 2005. Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. Clin. Endocrinol., 62: 487-491.

Leibel, R., M. Rosenbaum and J. Hirsch, 1995. Changes in energy expenditure resulting from altered body weight. N. Eng. Med. J., 332: 621-628.

Lellouch, J., H. Tran and J.L. Richard, 1973. La graisse d'une population masculine francaise active de 4000 sujets de 48-52 ans. Phatol. Biol., 21: 755-762.

Leonhardt, U., U. Ritzel, G. Schafer, W. Becker and G. Ramadori, 1998. Serum leptin levels in hypo- and hyperthyroidism. J. Endocrinol., 157: 75-79.

Lonnqvist, F., L. Nordfors and M. Schalling, 1999. Leptin and its potential role in human obesity. J. Int. Med., 245: 643-652.

Matzen, L.E. and J. Kventy, 1989. The influence of caloric deprivation and food composition on TSH, thyroid hormones and nuclear binding of T3 in mono nuclear blood cells in obese women. Metabolism, 38: 555-561.

Munan, L., A. Kelly, C. Petitclerc and B. Billon, 1978. Associations with body weight of selected chemical constituents in blood: Epidemiologic data. Clin. Chem., 24: 772-777.

Naslund, E., I. Andersson, M. Degerblad, P. Kogner, J.G. Kral, S. Rossner and P.M. Hellstrom, 2000. Association of leptin, insulin resistance and thyroid function with long-term weight loss in dieting obese men. J. Int. Med., 248: 229-308.

Niskanen, L., S. Haffner, L. Karhunen, A.K. Turpeinen, H. Miettinen and M.I. Unsitupa, 1997. Serum leptin in relation to resting energy expenditure and fuel metabolism in obese subjects. Int. J. Obes. Relat. Metab. Disord., 21: 309-313.

Papavramidis, S.T., A.C. Zisiadis, M.N. Keramouzis, I.I. Kessissoglou, H.A. Antoniadou and A.P. Aidonopoulos, 1995. Alterations in thyroid hormones and thyrotropin (TSH) in morbidity obese patients before and after vertical gastroplasty. Obes. Surg., 5: 298-301.

Rosenbaum, M., J. Hirsch, E. Murphy and R.L. Leibel, 2000. Effects of changes in body weight on carbohydrate metabolism, catecholamine excretionand thyroid function. Am. J. Clin. Nutr., 711: 1421-1432.

Roti, E., R. Minelli, M. Salvi, G. Simard, Y. Malthiery and V. Rohmer, 2002. Thyroid hormones and obesity. Ann. Endocrinol., 63: 135-139.

Sari, R., M.K. Balci, H. Altunba and U. Karayalcin, 2003. The effect of body weight and weight loss on thyroid volume and function in obese women. Clin. Endocrinol., 59: 258-262.

Sesmilo, G., R. Casamitjana, I. Halperin, R. Gomis and E. Vilardell, 1998. Role of thyroid hormones on serum leptin levels Eur. J. Endocrinol., 139: 28-430.

Matzen, L.E. and J. Kventy, 1989. The influence of caloric deprivation and food composition on TSH, thyroid hormones and nuclear binding of T3 in mono nuclear blood cells in obese women. Metabolism, 38: 555-561.

Wu, Z., U. Puigserver Pandersson, C. Zhang, G. Adelmant, V. Mootha, A. Troy, S. Cinti, B. Lowell, R.C. Scarpulla and B.M. Spiegelman, 1999. Mechanisms controlling mitochondrial biogenesis and respiration through the thermogenic coactivator PGG-1. Cell, 98: 115-124.

Yashkov, Y.I., L.I. Vinnitsky, M.V. Proykova and N.T. Vorobyova, 2000. Some hormonal changes before and after vertical banded gastroplasty for severe obesity. Obes. Surg., 10: 48-53.

Zimmermann-Belsing, T., G. Brabant, J.J. Holst and U. Feldt-Ramussen, 2003. Circulating leptin and thyroid dysfunction. Eur. J. Endocrinol., 149: 257-271.