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Alterations of Thyroid Functions in Obesity: Is There any Impact of Co-Existence of Type 2 Diabetes Mellitus?

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ABSTRACT

Aim: Little is known about the effect of coexistent type 2 diabetes mellitus (DM) on thyroid functions in obesity. We aimed to evaluate the thyroid function in the both diabetic and nondiabetic obese patients.

Materials and Methods: 145 obese patients admitted to our department, between June 2014 and May 2016, were included in the study. The patients with known thyroid dysfunction were excluded from the study. The patients were grouped according to their BMI (body mass index), co-existence of type 2 DM, and TSH (thyroid stimulating hormone). Data were collected retrospectively and analyzed.

Results: No difference was observed between diabetic and nondiabetic groups for the mean age, body weight, fT3 (free T3), fT4 (free T4), BMI, TSH. Primary hypothyroidism, subclinical hypothyroidism and hyperthyroidism were determined in 1.4, 0.7 and 2.8 % of the patients, respectively; no difference was found between diabetic and nondiabetic groups (p=0.588). There was no significant correlation between BMI and TSH (r=0.030, p=0.717).Distribution of patients in different TSH groups between diabetic and nondiabetic groups were similar (p=0.533). There were positive correlations between BMI and, fT4 or fT3 (r=0.274, p=0.001; r=0.280, p=0.002; respectively). Although 1.4% of all patients had isolated elevation of fT4, there was no difference between groups (p=0.178). 24.6% of diabetic, 28.4% of nondiabetic and 26.6% of all patients had isolated elevation of fT3; however, no difference was found (p=0.634).

Conclusions: Our study suggested that obesity could be associated with elevated fT4 and fT3. Elevation of fT3 and fT4 with increasing BMI may be as response to increased metabolic rate. We found no difference between diabetic and nondiabetic groups concerning to fT4 and fT3 elevation. As a result, co–existence of type 2 DM seems to have no effect on thyroid functions.

Key Words: *Obesity, Thyroid function, Diabetes mellitus*

Obezitede Tiroid Fonksiyonlarının Değişimi: Tip 2 Diabetes Mellitus'un Birlikte Varlığının Bir Etkisi var mı?

ÖZ

Amaç: Eşlik eden tip 2 diabetes mellitus (DM)'un obezitede tiroid fonksiyonları üzerindeki etkilerine ilişkin az şey bilinmektedir. Biz, diyabetik ve nondiyabetik obez hastalarda tiroid fonksiyonlarını değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Haziran 2014 ile Mayıs 2016 arasında kliniğimize başvuran 145 obez hasta çalışmamıza dahil edildi. Bilinen tiroid disfonksiyonu olan hastalar çalışmadan dışlandı. Hastalar vücut kitle indeksi (VKİ), eşlik eden tip 2 DM varlığı ve TSH (tiroid stimuli edici hormon) değerlerine göre gruplandırıldılar. Veriler retrospektif olarak toplandı ve analiz edildi.

Bulgular: Ortalama yaş, vücut ağırlığı, sT3 (serbest T3), sT4 (serbest T4), VKİ, TSH değerleri açısından diyabetik ve nondiyabetik gruplar arasında fark saptanmadı. Hastaların %1.4'ünde primer hipotiroidi, %0.7'sinde subklinik hipotiroidi ve %2.8'inde hipertiroidi saptandı; diyabetik ve nondiyabetik gruplar arasında fark saptanmadı (p=0.588). VKİ ile TSH arasında anlamlı bir korelasyon saptanmadı (r=0.030, p=0.717). Farklı TSH gruplarının diyabetik ve nondiyabetik gruplar arasındaki dağılımı benzerdi (p=0.533). VKİ ile sT4 veya

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sT3 arasında pozitif korelasyon mevcuttu (sırasıyla: r=0.274, p=0.001; r=0.280, p=0.002). Hastaların %1.4'ünde izole sT4 yüksekliği saptanırken, gruplar arasında anlamlı bir fark saptanmadı (0.178). Diyabetik grubun %24.6'sında, nondiyabetik grubun % 28.4'inde ve tüm hastaların % 26.6'sında izole sT3 yüksekliği saptandı; ancak gruplar arasında fark saptanmadı (p=0.634).

Sonuç: Çalışmamız obezitenin sT4 ve sT3 yüksekliği ile ilişkili olabildiğini destekledi. VKİ artışıyla sT3 ve sT4 değerlerinin artışı artmış metabolik hıza cevap olarak geilşebilir. Diyabetik ve nondiyabetik gruplar arasında sT4 ve sT3 yüksekliğine ilişkin bir fark saptanmadı. Sonuç olarak, eşlik eden tip 2 DM'nin varlığının tiroid fonksiyonları üzerinde etkisi izlenmedi.

Anahtar Sözcükler: *Obezite, Tiroid fonksiyonu, Diabetes mellitus*

INTRODUCTION

Obesity is a pandemic disease threatening public health especially in the industrialized world, and its prevalence is increasing worldwide. In Turkey, its prevalence was 35.9% in 2010 according to TURDEP II study (1). A lot of comorbidities regarding to different organ systems may be associated with obesity, and some of them exist as a part of metabolic syndrome, like dyslipidemia, insulin resistance or diabetes mellitus.

Alterations of thyroid functions have become one of the most frequent endocrinopathies. The functions of thyroid gland may be affected by drugs, systemic disorders, pregnancy, or disorders involving primarily the gland itself. Recently, it has been thought that thyroid functions could be influenced by obesity itself. Similar to obesity, diabetes mellitus has been thought to have an effect on thyroid functions. However, limited data exists concerning the influence of obesity and diabetes mellitus on thyroid functions. We aimed to determine the alterations of thyroid functions and the effect of co-existence of diabetes mellitus on thyroid functions in obese patients.

MATERIALS and METHODS

145 obese patients admitted to our department, between June 2014 and May 2016, were included in the study. Obese patients with or without diabetes mellitus were included in the study. The patients with known thyroid dysfunction were excluded from the study. The patients were grouped according to the co-existence of type 2 diabetes mellitus: diabetic obese patients (n=69) and nondiabetic obese patients (n=76). The patients were also grouped as regards to BMI (body mass index) levels: BMI<40 kg/m^2 (n=7), BMI between 40 and 49.99 kg/m^2 (n=69), BMI between 50 and 59.99 kg/m^2 (n=42), BMI>60 kg/m^2 (n=27). Clinical and laboratory data of the patients were analyzed retrospectively. We grouped our patients also according to their TSH (thyroid stimulating hormone) levels: TSH lower than lower limits of normal, TSH in normal range, TSH higher than upper limits of normal. Parameters of TSH, fT3(free T3), fT4(free T4) were measured with chemiluminescence method by using the Beckman Coulter marked and DxI 800 model device (Beckman Coulter, Inc. 4300 N. Harbor Blvd., Fullerton, CA 92835 U.S.A.). Normal reference ranges of parameters were as follow: TSH 0.5-4.5 μIU/mL, fT3 1.9-4.2 pg/mL, fT4 0.61-1.32 ng/dL. Our study was compatible with principles of Helsinki declaration. Ethical approval was obtained from local ethics committee, and written informed consent forms were taken from each patient.

SPSS 17.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of data. We used Shapiro-Wilk test to assess the compatibility of data with normal distribution. Homogeneity of variance was evaluated by Levene test. When comparing independent two groups according to quantitative data, Independent-Samples T test was used with Bootstrap results, Mann-Whitney U test was used with Monte Carlo stimulation technique. In comparison of categorical variables each other, Pearson Chi-Square test was used with Exact and Monte Carlo stimulation results. Pearson correlation(r) analysis was used for correlation among variables. Quantitative variables were defined as mean±standard deviation (minimum-maximum) in the tables. Categorical variables were shown as number (n) and percent (%). Variables were analyzed at 95% confidence level and p value <0.05 was accepted as significant.

RESULTS

The clinical and demographic parameters of the patient groups were given in Table 1. There was no statistically significant difference between diabetic and nondiabetic obese groups for mean values of age, body weight, fT3, fT4 (p=0.134, p=0.151, p=0.206, and p=0.579; respectively). There were no significant differences between two groups according to mean values of BMI or TSH (p=0.623 and p=0.937; respectively).

Distribution of patients in different BMI groups between diabetic and nondiabetic obese patients were different (p=0.012). 23.2% of diabetic obese and 14.5% of nondiabetic obese patients had BMI value of greater than 60 kg/m^2. Distribution of the patients in different TSH groups between diabetic and nondiabetic obese patients were similar (p=0.533). 1.4% of all patients had isolated elevation of fT4 levels, and there were no statistically significant differences between diabetic and nondiabetic groups (p=0.178). 26.6% of total, 24.6% of diabetic obese, and 28.4% of nondiabetic

obese patients had isolated elevation of fT3 levels. There were no statistically significant difference between diabetic and nondiabetic groups in regard to fT3 level elevation (p=0.634) (Table2).

Primary hypothyroidism, subclinical hypothyroidism and subclinical hyperthyroidism were determined in 1.4, 0.7 and 2.8% of the patients respectively; there were no statistically significant difference between diabetic and nondiabetic groups (p=0.588) (Table 3).

There were no significant difference for TSH levels between different BMI groups (p= 0.446). There were significant differences according to fT3 and fT4 levels between BMI groups (p=0.030, and p=0.027; respectively). fT4 levels were found to be higher in the group of BMI> 60kg/m^2 than BMI between 40 and 50 kg/m^2 (p<0.05) (Table 4).

There were significant positive correlations between BMI and free T4 levels, and also free T3 levels (r=0.274, p=0.001; and r=0.280, p=0.002; respectively). There were no significant correlation between BMI and TSH (p=0.717). No significant correlation between age and BMI values were observed (p=0.237). Correlations were demonstrated in Table 5.

Table 1: The clinical and demographic parameters of the patient groups

Parameter	Diabetic obese (n=69) mean±SD (min.-max.)	Nondiabetic obese (n=76) mean±SD (min.-max.)	p value
Age	45.57±8.95 (24-74)	36.95±10.39 (18-63)	0.134
Body weight (kg)	127.33±22.27 (90-202)	125.41±18.57 (94-182)	0.151
BMI (kg/m^2)	45.72±7.09 (26.5-64)	44.77±4.31 (40-56)	0.623
TSH	2.03±1.13 (0.42-6.75)	2.03±1.28 (0.07-8.84)	0.937
fT4	1.03±0.17 (0.64-1.65)	0.96±0.19 (0.52-1.76)	0.579
fT3	3.84±0.86 (2.34-7.37)	3.81±0.66 (2.81-5.55)	0.206

Table 2: Comparison of fT3 levels between groups

Groups	Normal fT3 level n (%)	Elevated fT3 level n (%)	Total n (%)	p value
Diabetic obese	43 (75.4)	14 (24.6)	57 (100)	
Nondiabetic obese	48 (71.6)	19 (28.4)	67 (100)	0.634
Total	91 (73.7)	33 (26.6)	124 (100)	

Table 3: Comparison of the distribution of thyroid dysfunction

Groups	Euthyroid n (%)	Primary hypothyroidism n (%)	Subclinical hypothyroidism n (%)	Subclinical hyperthyroidism n (%)	Total n (%)	p value
Diabetic obese	66 (95.7)	1 (1.4)	1 (1.4)	1 (1.4)	69 (100)	
Nondiabetic obese	72 (94.7)	1 (1.3)	0 (0.0)	3 (3.9)	76 (100)	0.588
Total	138 (95.2)	2 (1.4)	1 (0.7)	4 (2.8)	145 (100)	

Table 4: Comparison of thyroid hormones between BMI groups

BMI groups	TSH mean±SD (n)	p value	fT4 mean±SD (n)	p value	fT3 mean±SD (n)	p value
<40 kg/m^2	1.71±0.56 (7)		0.93±0.19 (7)		3.47±0.80 (7)	
40-50 kg/m^2	2.18±1.44 (69)		0.96±0.19 (69)		3.66±0.61 (58)	
50-60 kg/m^2	1.76±.89 (42)	p=0.446	1.01±0.13 (42)	p=0.027	4.00±0.90 (37)	p=0.030
>60 kg/m^2	2.17±1.04 (27)		1.08±0.20 (26)		4.08±0.71 (22)	
Total	2.03±1.20 (145)		0.99±0.18 (144)		3.82±0.75 (124)	

Table 5: Correlations between thyroid hormones and age, body weight, height, and BMI

		TSH	fT4	fT3
Age	r	-0.204	0.043	-0.137
	p	0.014	0.610	0.129
	n	145	144	124
Body weight	r	-0.025	0.107	0.227
	p	0.769	0.201	0.011
	n	145	144	124
Height	r	-0.040	-0.120	-0.011
	p	0.630	0.152	0.905
	n	145	144	124
BMI	r	0.030	0.274	0.280
	p	0.717	0.001	0.002
	n	145	144	124

DISCUSSION

Our results suggest that obesity may be associated with elevated fT4 and fT3 levels. It may be considered that elevation of fT3 and fT4 levels with increasing BMI could be a response to increased metabolic rate. According to our results, there were no statistically significant difference between diabetic and nondiabetic groups when comparing elevated fT4 and fT3 levels. As a result, co–existence of type 2 diabetes mellitus seems to have no effect on thyroid functions.

In population-based studies, the prevalence of subclinical hypothyroidism and overt hypothyroidism were determined as 4-15 % and 0.1-2%, respectively (2-7). In our study, we observed less frequent subclinical hypothyroidism (0.7%) in our obese patients. Likewise, Montoya-Morales et al. showed higher frequencies of primary and subclinical hypothyroidism (8% and 6%; respectively) comparing to our results (8). Bouglé et al. found a higher frequency of subclinical hypothyroidism among the obese subjects (13% of 528 obese subjects) (9). Michalaki et al. also determined high prevalence of overt and subclinical hypothyroidism in morbidly obese patients (19.5% in 144 patients) (10). These findings showed that the frequency of hypothyroidism and subclinical hypothyroidism was variable in different cohorts.

In our study, we found positive correlations between BMI and, fT4 or fT3 levels; however, there was no significant correlation between TSH and BMI. Some studies investigated normal population as well as the obese patients. A cross sectional population study done by Knudsen et al. showed us findings in contrast to our results, in normal euthyroid population including 4082 euthyroid subjects (11). In this study, subjects were categorized as serum TSH or fT4 concentrations. Positive association between BMI and category of TSH, negative association between BMI and category of fT4, and no association between BMI and fT3 were found in this study. Michalaki et al. determined higher levels of T3, T4, fT3, TSH levels in morbidly obese subjects(10). Muscogiuri et al. showed there was no difference regarding to fT3 and fT4 levels between overweight/obese and lean subjects in their study, including 60 healthy euthyroid subjects (12). Another study including 1572 euthyroid appearingly healthy women, done by Shon et al., determined that fT4 was negatively correlated with BMI in contrast to our study (13). Similar to our findings, there were no significant association between TSH and BMI in that study. Iacobellis et al. determined statistically positive correlation between TSH and BMI in their study including 87 uncomplicated obese euthyroid women (14). Manji et al. also investigated an association between thyroid function and the body mass index in 401 euthyroid subjects (15). There were no statistically significant correlation between BMI and serum TSH, and fT4 in this study.

As a result of these studies, we may say that BMI seems to be associated with the changes in thyroid status, even within normal range. We think that this association may be reciprocal. Alterations in thyroid function may affect the body mass index, due to direct effects of thyroid hormones, as seen in hypothyroidism (weight gain) and thyrotoxicosis (weight loss). BMI also may influence thyroid status, by changing basal metabolic rate and metabolic needs of the tissues.

We suggest that other metabolic parameters may be included in studies designed to relieve thyroid function status in obese patients. Kommareddy et al. reported the study to assess an association between TSH level and metabolic syndrome in obese and overweight patients (16). In that study, no statistically significant association were determined between the TSH levels and the metabolic syndrome.

In conclusion, our study suggests that obesity may be associated with elevated fT3, and fT4 levels. The co-existence of diabetes mellitus seems not to be effective on thyroid functions in obese patients. To investigate the effect of diabetes mellitus on thyroid functions in obese patients, further studies including healthy subjects are necessary.

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