ORIGINAL ARTICLE

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Evaluation of Thyroid Ultrasound and Thyroid Hormone Levels in Obese Patients who applied to the Outpatient Clinic of Family Medicine

ABSTRACT

Objective: In the present study, we aimed to evaluate obesity in terms of its effect on thyroid function and morphology.

Methods: We included 327 consecutive obese patients (mean age 41.0±11.6) who applied to the Department of Family Medicine Obesity and Check-up Polyclinic of Düzce University School of Medicine and had an ultrasound scan (USG) between the months January to July 2012. Cases were classified as patients with obesity (n=130), patients with Type 2 Diabetes mellitus (DM) (n=27) and patients with Metabolic Syndrome (METS) (n=170). USG findings, as well as hematological, biochemical and hormonal parameters, were compared among these groups

Results: When body mass index (BMI) values were compared between the groups, the highest results were found in DM group, and these results were statistically significant. In USG examinations of patients, 108 (29.2%) patients had nodules. There was no difference between the groups in terms nodule prevalence. When thyroid volumes were compared between the groups, the largest volumes were found in the DM group; however, this was statistically not significant. When thyroid stimulating hormone (TSH) levels were compared, the highest levels were in the obesity group; however, these results were again statistically insignificant. We observed that obese women and women with METS had higher TSH levels. Thyroid disorders were found less frequent in the DM group than the other groups, and these results were statistically significant.

Conclusion: Although no significant difference was found between the groups in our study in terms of thyroid pathology, in the light of other studies, the prevalence of thyroid dysfunction in diabetic patients and patients with METS is 2-3 times higher than the normal population. Therefore the measurement of TSH should be made for all obese patients.

Keywords: Obesity, Metabolic Syndrome, Insulin Resistance, Thyroid Nodule

Aile Hekimliği Polikliniğine Başvuran Obez Hastaların Tiroid Hormon Düzeylerinin ve Tiroid Ultrasonlarının Değerlendirilmesi

ÖZ

Amaç: Mevcut çalışmamızda obeziteyi, tiroid fonksiyon ve morfolojisi üzerinde oluşturduğu değişiklikler açısından incelemeyi amaçladık.

Yöntem: Düzce Üniversitesi Tıp Fakültesi Aile Hekimliği Anabilim Dalı Check-up ve Obezite Polikliniğine 2012 Ocak-Temmuz ayları arasında başvuran ve ultrasonografi taramasından geçirilen yaş ortalaması 41,0±11,6 yıl olan, 327 ardışık obez olgu alındı. Olgular: Obez (n=130), Metabolik Sendrom (METS) (n=170) ve tip 2 Diyabet (DM) (n=27) gruplarına ayrılarak ultrasonografi bulguları, hematolojik ve biyokimyasal parametreler ile tiroid fonksiyonlarının karşılaştırması yapıldı.

Bulgular: Gruplar arası vücut kitle indeksi değerleri incelendiğinde, en yüksek değerler DM'li grupta tespit edilmiş olup, istatistiksel olarak anlamlı bulunmuştur. Olguların ultrasonografi sonuçlarına göre, 108 (%29,2) olguda nodül saptanmıştır, gruplar arasında nodül bulunma sıklığı açısından fark saptanmamıştır. Tiroid hacmi gruplar arasında değerlendirildiğinde, en büyük volümler DM'li grupta tespit edilmiş olup istatistiksel olarak anlamlı bulunmamıştır. Gruplarda tiroid stimulan hormon (TSH) düzeyleri incelendiğinde en yüksek değerler obez grupta olup istatistiksel olarak anlamlı bulunmamıştır. Obez ve METS'li kadınlarda TSH düzeylerinin daha yüksek olduğu görülmektedir ve DM grubunda tiroid bozukluklarının diğer gruplardan daha nadir görülmesi istatistiksel olarak anlamlı bulunmuştur.

Sonuç: Bizim çalışmamızda tiroid patolojisi açısından gruplar arasında anlamlı fark saptanmamakla birlikte yapılan çalışmaların ışığında METS ve diyabetik hastalarda tiroid disfonksiyonu saptanma oranı normal populasyona göre 2-3 kat yüksektir. Bu nedenle, tüm obez hastalarda TSH ölçümü yapılmalıdır.

Anahtar Kelimeler: Obezite, Metabolik Sendrom, İnsülin Direnci, Tiroid Nodülü

INTRODUCTION

In recent years, obesity prevalence increases all over the world. Epidemiological studies demonstrated that nutrition habits; genetic, environmental, neurological, physiologic, biochemical, psychological factors and life style factors like cigarette and alcohol consumption, lack of physical activity as well as demographic factors like age, gender; sociocultural factors like level of education and marital status are responsible for obesity. According to World Health Organization (WHO) data, overweight affects 30-80% of adults in Europe, and 20% of children and adolescents are overweight, whereas one of third of these are obese. In addition, overweight and obesity in adults is responsible for 35% of ischemic heart diseases, 55% of hypertension, 80% of type 2 diabetes mellitus (DM) cases and more than one million deaths per year in Europe (1-5).

Obesity, especially central obesity, is related with a lot of endocrine abnormalities including thyroid dysfunction. Besides regulating the energy metabolism and thermogenesis, triiodothyronine (T_3) plays a critical role in glucose and lipid metabolism, nutrition intake and fatty acid oxidation. In addition thyroid dysfunction is related to body temperature, changes in body weight and composition, basal energy expenditure independent from total and physical activity (4,6,7).

Obesity generally is related closely to insulin resistance; glucose and fatty acid utilization of peripheral tissues and it is one of the important causes accused for metabolic syndrome (METS) and DM development. Studies performed in recent years suggest that some hormonal and humoral mediators released from the adipose tissue stimulated the hypothalamo-hypophyseal-thyroid axis and increased thyroid stimulating hormone (TSH) secretion. It was demonstrated that components of METS and insulin resistance were significantly associated with decreased free thyroxin (fT_4) and/or increased TSH levels within euthyroid limits. Basic mechanism that is emphasized is that there is an association between thyroid hormones and leptin (4-6).

Palpable thyroid nodules are found in 4-7% of the population and nodules are detected incidentally on ultrasonography in 19-67% of the population. A lot of nodules are asymptomatic and a lot of people with nodules are euthyroid. Because 5% of palpable nodules are malignant, main purpose in evaluation of thyroid nodules is ruling out malignancy (7-9).

The purpose in this study was to determine thyroid hormone levels and thyroid gland structural changes in patients who applied to our obesity and check-up polyclinic and who DM, METS and insulin resistance together with obesity.

MATERIAL AND METHODS

In this cross sectional and descriptive study, we included 327 consecutive obese patients (mean age 41.0±11.6) who applied to the Department of Family Medicine Obesity and Check-up Policlinic of Düzce University School of Medicine and had an ultrasound scan (USG) between the months of January and July of 2012. Cases were divided in three groups; obesity group (n=130), metabolic syndrome group (METS) (n=170) and DM type 2 (n=27) group, according to WHO description of obesity, ATP-3 and ADA guide (2,10-13). Thyroid morphology was evaluated by using ultrasound findings, hematological and biochemical parameters. Anthropometric measurements and sociodemographic data of all included patients were recorded.

Non-invasive Clinical Ethics*:** The ethics of the study was approved by Non-invasive Clinical Ethic committee of Duzce University Medical Faculty (date of 02/08/2013 and Ethic No: 2013/421***) and was performed in accordance with the ethical standards laid down in the Declaration of Helsinki (1964).

Biochemical analyses: All measurements were made at the biochemistry laboratory of Duzce University Research Hospital. Complete blood counts were measured with the automatic blood count device CELL-DYN 3700 SL (Abbott Diagnostics, Chicago, USA). Serum iron, unsaturated iron binding capacity (UIBC), ferritin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose, calcium, phosphorus, urea, uric acid analysis and urine albumin and urine creatinine analyses were made at a single session by using Cobas 6000 (Roche Diagnostics GmbH, Mannheim, Germany) auto analyzer commercial kits.

Serum TSH, T_3, T_4 hormones, insulin and high sensitive-CRP measurements were made at a single session with the auto analyzer Siemens IMMULITE 2000 (Siemens Healthcare Diagnostics Inc. Flanders NJ. USA) used by original kits and chemiluminescence's enzyme immunoassay. Periodic internal and external quality-controls were made to detect probable errors that may influence test results of biochemical analyses.

***HOMA-IR Value Calculation*:** It was calculated with the formula of HOMA (homeostasis model assessment formula) which reflects insulin resistance.

HOMA= Serum fasting glucose (mg/dL) x fasting plasma insulin level (μU/mL)/ 405

A HOMA-IR value greater than 2.7 was accepted as insulin resistance.

***Metabolic Syndrome and Obesity Determination*:** WHO (2) definition was used for obesity. *BMI= Body weight (kg)/ (height)² (m^2).* BMI >29.9 kg/m^2 was accepted as obesity.

Waist circumference was measured around the belly, and hip circumference was measured around the pubis and the most prominent part of the buttocks.

NCEP ATP III (10,11) definition was used for Metabolic Syndrome. The presence of 3 out of the following 5 criteria was accepted as Metabolic Syndrome:

1. *Fasting blood glucose ≥110 mg/dL*
2. *Triglyceride level ≥150 mg/dL*
3. *HDL-C < 50 mg/dL*
4. *Waist circumference: >88 cm for women, >94 cm for men*
5. *Blood pressure: ≥130/85 mmHg*

***Ultrasonography*:** B-mode thyroid ultrasonography was performed by using a4-10 MHz superficial linear probe of the GE LOGIQ 5 PRO A 11 L ultrasound device present at the Family Medicine Policlinic (*by two training Sonography personnel*). Thyroid volumes were calculated by measuring the lengths in three dimensions multiplied by 0,523 according to ellipsoid formula (14,15). The structure (purely solid, mixed), echogenity (hypo-, iso-, hyper echoic and heterogeneous), contours (regular, irregular, lobulated), presence of calcifications and other characteristics of the nodules were recorded.

***Statistical Analysis*:** Statistical analyses were made with SPSS statistics programme (SPSS, Chicago, IL, USA, version 11.5). Student's t-test was used for the significance of differences between averages, One Way ANOVA (Bonferroni) test for multiple groups and Chi- square (Fisher's exact) test for categorical variables. Correlation between measurements were evaluated with Pearson Correlation Analysis, parameters that have no normal distribution were evaluated with Spearman's Rho Correlation Test. Results were given in 95% confidence interval, averages were given as ± standard deviation. P values <0.05 value were accepted statistically significant in tests used.

RESULTS

In the study, we included 327 patients (between ages 18-70) that fulfilled the obesity criteria according to WHO description. Patients were evaluated in 3 groups; metabolic syndrome group (METS) (n=160; 145 women, 25 men), DM group (n=27; 24 women, 3 men) and obesity only group (n=130; 118 women, 12 men) according to ATP III and ADA criteria.

There was no difference between METS group and other groups regarding TSH, fT_4, WBC, Hemoglobin (HB), Htc, PLT count and thyroid volumes on ultrasound (p>0.05). Age (p<0,0001), BMI (p<0,0001), waist (p<0,0001), hip (p<0,0001), systolic blood pressure (SBP) (p<0,0001), diastolic blood pressure (DBP) (p<0,0001), uric acid (p<0,0001), HOMA-IR (p<0,0001), insulin (p<0,0001) and Triglyceride (TG) (p<0,0001), Total Cholesterol (p=0,027) and LDL (p=0,020) levels in DM and METS were significantly higher than in obese group and HDL levels were significantly lower (p<0,0001). As expected in the DM group, glucose was significantly higher than in obese and METS groups (Table 1).

When thyroid functions were compared between groups, there were 117 (90%) euthyroid, 10 (7.7%) hypothyroid and 3 (2.3%) hyperthyroid persons in the obesity group; 150 (88.2%) euthyroid, 13 (7.6%) hypothyroid and 7 (4.2%) hyperthyroid persons in METS group; 26(96.3%) euthyroid and one (3.7%) hypothyroid in DM group. There were significantly less thyroid diseases in the DM group than in other groups (p=0,017) (Table 2).

According to USG results of patients, 108 (%29.2) patients had nodules. There was no difference between the groups in terms of nodule frequency. When number of nodules were compared, it was remarkable that single nodules were more frequent in obesity and METS groups, whereas multiple nodules were more frequent in the DM group.

Nodule frequency in the METS group was higher than in other groups and these nodules were of solid character. In addition, calcification (14.8%) in nodules was more prevalent in DM group (p=0.014). Regarding the nodule size, nodules smaller than 15 mm of diameter were significantly more common in METS group and nodules greater than 15 mm of diameter were significantly more common in DM group (p=0.004) (Table 3).

Table 1. Demographic parameters of each group

Parameters	**OBESE** **n=130**	**METS** **n=170**	**DM** **n=27**	**Total** **n=327**	p
Age (yr)	38.1±11.6	42.1±11.1	48.3±10.4	41.0±11.6	<0.0001
BMI (kg/m^2)	33.9±5.6	37.8±6.4	40.0±7.4	36.4±6.4	<0.0001
Waist (cm)	100.1±12.2	108.7±12.5	111.3±13.1	105.5±13.2	<0.0001
Hip (cm)	118.6±11.1	124.4±12.4	126.1±12.3	122.2±12.2	<0.0001
Systolic BP (mmHg)	121.2±14.3	133.0±19.0	137.8±14.4	128.7±18.0	<0.0001
Diastolic BP (mmHg)	78.7±11.5	86.2±12.8	89.8±11.3	83.5±12.8	<0.0001
Thyroid volume (mL)	12.2±5.9	11.9±3.8	12.9±3.4	12.1±4.7	0.524

***METS**, Metabolic Syndrome; **DM**, Diabetes Mellitus; **BMI**, Body Mass Index; **BP**, Blood Pressure.*

Table 2. Hematological, biochemical and hormonal parameters of groups

Parameters	OBESE n=130	METS n=170	DM n=27	Total n=327	p
WBC (x1000 µL)	7.2±1.7	7.4±1.8	7.6±1.6	7.3±1.7	0.353
HB (g/dL)	13.2±1.3	13.5±1.4	13.1±1.4	13.4±1.3	0.178
HTC (%)	39.9±3.6	40.4±4.0	39.2±3.5	40.1±3.8	0.191
PLT (x1000 µL)	281.7±64.6	294.0±77.0	273.5±55.9	287.4±70.9	0.194
Glicose (mg/dL)	93.8±9.2	100.4±18.7	139.2±40.2	101.0±22.0	<0.0001
Uric acid (mg/dL)	4.3±0.9	5.2±1.2	5.1±1.2	4.8±1.2	<0.0001
ALT (U/L)	18.2±10.6	23.4±17.0	22.3±11.9	21.3±14.6	0.007
AST (U/L)	18.8±5.7	22.7±10.2	22.4±7.5	21.1±8.7	<0.0001
TG (mg/dL)	103.7±37.6	156.4±68.3	139.3±40.9	133.7±61.0	<0.0001
Total Cholesterol (mg/dL)	191.3±39.4	204.0±42.5	195.7±29.1	198.2±40.7	0.027
HDL Cholesterol (mg/dL)	55.0±11.6	46.7±11.0	47.8±8.2	50.1±11.7	<0.0001
LDL Cholesterol (mg/dL)	115.7±32.5	126.9±36.1	120.0±26.5	121.8±34.3	0.020
HOMA-IR	2.5±1.4	4.0±1.8	-	3.3±1.8	<0.0001
Insulin (µU/mL)	10.6±5.7	16.3±7.7	13.4±4.3	13.8±7.4	<0.0001
TSH (mIU/L)	2.2±1.9	2.1±1.9	1.5±0.7	2.1±1.8	0.260
fT_4 (pmol/L)	1.1±0.5	1.0±0.2	1.1±0.2	1.1±0.3	0.528

Table 3. The results of thyroid ultrasound examination and features

	OBESE n(%)	METS n(%)	DM n(%)	Total n(%)	p
Gender					0.351
Female	118 (90.8)	145 (85.3)	24(88.9)	287(87.8)	
Male	12 (9.2)	25(14.7)	3(11.1)	40(12.2)	
Function					0.017
Euthyroid	117 (90)	150 (88.2)	26 (96.3)	293(89.6)	
Hypothyroid	10 (7.7)	13 (7.6)	1 (3.7)	24(73)	
Hyperthyroid	3 (2.3)	7 (4.2)	0	10(3.1)	
Parenchyma					
Homogenic	99(76.1)	131(77)	22(81.5)	252(77)	0.862
Heterogenic	31(23.9)	39(23)	5(18.5)	75(23)	
Calcification					0.014
Yes	3(2.3)	7(4.1)	4(14.9)	14(4.3)	
No	127(97.7)	163(95.9)	23(85.1)	313(95.7)	
Nodule					0.343
Yes	37 (28.5)	62 (36.5)	9 (33.3)	108 (33)	
No	93 (61.5)	108 (63.5)	18 (66.7)	219 (67)	
Nodule size					0.004
<15 mm	22 (16.9)	35 (20.6)	4 (14.8)	61(18.7)	
≥15 mm	15 (11.5)	27 (15.9)	5 (18.5)	47(14.3)	
No Nodule	93(71.6)	108(63.5)	18(66.7)	219(66.7)	
Number of Nodules					0.225
No Nodule	93(71.5)	108(63.5)	18(66.7)	219(67)	
1	16(12.3)	39(22.9)	3(11.1)	58(17.7)	
2	12(9.3)	10(5.9)	1(3.70)	23(7)	
3	6(4.6)	7(4.2)	3(11.1)	16(4.9)	
≥4	3(2.3)	6(3.5)	2(7.40)	11(3.4)	
Type of Nodules					0.317
No Nodule	93(71.5)	108(63.5)	18(66.7)	219(67)	
Solid	24(18.5)	47(27.7)	6(22.2)	77(23.5)	
Cystic	6(4.6)	12(7)	2(7.4)	20(6.1)	
Complex	7(5.4)	3(1.8)	1(3.7)	11(3.4)	
Total	**130**	**170**	**27**	**327**	

DISCUSSION

In thyroid nodules evaluation TSH measurement and thyroid USG are accepted methods all over the World in primary care. In studies published in recent years it was reported that some humoral and hormonal mediators released from adipose tissue stimulated hypothalamo-hypophyseal-thyroid axis and increased TSH secretion. Main mechanism suspected is a probable relation between leptin and thyroid hormones. It was reported that there is positive correlation between BMI and thyroid gland volume, however a causal connection wasn't manifested (14,16-18).

In the study of Aytürk et al (14) it was confirmed that serum TSH raise was an independent risk factor regarding thyroid volume increase in patients with METS. In addition it was observed that thyroid volume increase is significantly related to all components of METS and IR, statistically significant relationship between thyroid volume and waist circumference (WC), TG, IR continues. On the other hand no relation was established between thyroid nodule formation and TSH. However a significant relation was observed between thyroid nodule formation and four components of METS (WC, FBG, HT, and TG) and IR. It was shown that among other variables that might contribute to nodule formation, ID was associated with increase in nodule formation but TSH had no such association.

Estimated relative risk of IR on thyroid nodule formation over absence of IR was determined as 3.2 (GA 95%). Aytürk's findings support that thyroid nodule formation in METS patients may develop with a mechanism independent from TSH, although thyroid volume increase is associated with serum TSH increase in these patients. It is known that insulin- IGF-1 pathway modulates the regulation of thyroid gene expression and in addition this pathway is thought to be an important co-factor effective on thyrocyte proliferation and differentiation (19-21).

In the present study a negative correlation with a slight significance was found between thyroid volume and TSH levels (r=-0.167, p=0.002). As the thyroid functions of the groups are examined, it is seen that 117 people have euthyroid (90%), ten have hypothyroid (7.7%) and three have hyperthyroid (2.3%) in the obese group, 150 have euthyroid (88.2%), 13 have hypothyroidism (7.6%), seven have hyperthyroidism (4.2%) in the METS group and 26 have euthyroid (96.3%) and only one has hypothyroidism (3.7%); and the lower rate of thyroid disease in the DM group was found to be statistically significant (p=0.017). When the TSH levels of the groups were compared, it was seen that the highest level of TSH was detected in the obese group and it was found to be statistically significant (2.2±1.9; p=0.260). However, the TSH levels of the women in the obese and METS groups were found higher. The highest levels of Ft4 were seen in the group with DM, especially males, but it was statistically significant. As the thyroid volumes were compared among the groups, the highest volumes were detected in the group with DM and it was not found to be statistically significant (12.9±3.4 p=0.524). Although the volume of the thyroid gland was found to be positively related to BMI in the previous studies, we did not detect a significant relationship in our study.

The frequency of thyroid nodules increases with age. It is seen 2-4 times more in females when compared to males. In the largely populated Framingham study done by Vander et al. (22), the female/male ratio was found to be 4.2/1.0.

In the study of Erdogan et al (23), nodular goiter was detected in 26.4% of the females and in 20.5% of the males in a group of 2025 patients between the ages of 18-65 by the use of thyroid ultrasonography; however, these rates were seen to reach 48% in females and 38% in males between the ages of 55-65. In our study, the frequency of thyroid nodules increased with age (r=0.185; p=0.001) and it was more commonly seen in women (n=101, 35.2%) as compared to men (n=7, 17.5%). In a study done on morbidly obese women, the prevalence of thyroid nodules in normal weight and mildly overweight women were compared and the number and frequency of nodules was found to be significantly lower in the morbidly obese (24).

However, in Kömürcü's (25) thesis study in which he evaluated 170 morbidly obese patients in the endocrinology clinic, the results of a thyroid USG revealed nodules in 56.2% of the patients. 84.9% of them were multiple and 15.1% of them were solitary nodules. The presence and the type distribution of the nodules were found to be similar and there was no statistically significant difference between the frequency of nodules and the ratios of their types according to BMI classifications. The reason behind the increased rate of nodule detection was thought to be the fact that Kömürcü (25) performed his study on a chosen group of patients in the Endocrinology and Metabolism Diseases polyclinic.

According to the USG results of our study, 108 cases (33%) had nodules and there was no difference in terms of the frequency of nodules between the groups. Solitary nodules were more commonly seen in obese and METS groups, whereas multiple nodules were seen more frequently in the DM group despite the fact that the frequency of the nodules was less than the other two. Calcification in the nodules seen more commonly in the DM group (14.8%) in USG (p=0.014). When compared according to the size of the nodule, nodules <15 mm were seen more commonly in the METS group and those ≥15 mm were more commonly seen in the DM group (p=0.004) (Table 3).

In a previous study done on type 2 DM and METS patients, a positive correlation was detected between BMI and both SBP and DBP. It was determined that CBP, BMI, FGL, Total Cholesterol/HDL Cholesterol increase with age. A positive correlation was detected between H/W ratio and BMI values and H/W ratio and TG values (26).

Tanyeri et al. (27) found the systolic and diastolic blood pressures to be statistically significantly higher in women than in men ($p<0.01$). In the study, they conducted on a total of 420 people, 210 women and 210 men in order to research obesity prevalence. 43.7% of the obese individuals were found to be hypertensive and 86.3% of the hypertensive people were found to be obese, and the relationship between BMI and the systolic ($r=0.45$, $p<0.001$) and diastolic ($r=0.44$, $p<0.001$) blood pressures were found to be statistically significant.

In our study, when the SBP and DBP were compared between the groups, it was seen that the DM group had the highest values (137.8±14.4 $p<0.0001$; 89.8±11.3, $p<0.0001$ respectively) and it was found statistically significant. When the groups were examined according to gender, it was seen that SBP peeks in women with METS and DM. Meanwhile, DBP is highest in women with DM. Also, there were strong positive correlations between waistline measurements and SBP ($r=0.422$, $p<0.0001$) and DBP ($r=0.384$, $p<0.0001$).

In the study of Ozkan et al (28) on 276 patients with diabetes, the mean total cholesterol was 217.4±46.4 mg/dL, LDL cholesterol was 147.1±36.7 mg/dL, TG: 216.6±16.6 mg/dL, HDL cholesterol was 45.3±9.4 mg/dL. The LDL levels were found to be optimum in 24 patients (8.7%), acceptable in 67 patients (24.3%), borderline high in 86 patients (31.2%), high in 65 patients (23.6%) and very high in 34 patients (12.3%). Upon taking history, it was learnt that 247 patients (89.4%) were previously told they had high lipid levels and given treatment but only 156 of them use their lipid lowering medications regularly and do not comply with the diet.

Upon comparing the TG levels between the groups, it was found out that the group with METS had the highest levels and it was found to be statistically significant (156±68.3 p<0,0001). Also, there was a significant positive correlation between HOMA-IR and TG ($r=0.499$, $p<0.0001$). The METS group had the highest total cholesterol and LDL levels (204.0±42.5, $p=0.027$, 126.9±36.1, $p=0.020$ respectively). The highest values were observed in the men of the METS group. The lowest levels of HDL were observed in the METS group as well and it was statistically significant (46.7±11.0 $p<0.0001$). A decrease in HDL levels draws attention, especially in men with DM and METS.

In the 76 obese women with BMIs over 28 whom Özinan et al (29) grouped according to the presence of ID, the HDL cholesterol levels were significantly lower in the ID+ group ($p=0.043$), but the triglyceride and uric acid levels were significantly lower as well ($p= 0.032$ and $p= 0.032$ respectively). There was no difference between the ID+ and ID- groups according to age, BMI, waistline measurements and waist/hip ratios but the weight of ID+ obese were found to be higher than that of ID- obese ($p=0.033$).

In a study done on Brazilian adolescents with type 2 DM risk factors, the subjects were grouped into normal weight, overweight and obese. No statistically significant difference was found according to age, gender, race distribution, height, birth weight, Total Cholesterol, LDL, HDL, fasting plasma glucose and the 2nd hour plasma glucose levels, but the SBP levels (129.29±14.96 mmHg; $p<0.001$), TG levels (99.61±36.97 mg/dL; $p<0.01$), 2nd hour insulin levels (73.09±39.82 μIU/mL; $p<0.001$) and finally, HOMA-IR levels (3.14±1.89; $p<0.001$) were statistically significantly higher in the obese group. Also, the normal weight group had lower uric acid levels when compared to the other two groups (4.19±1.0 vs. 4.9±0.32 vs. 5.08±1.49 mg/dL respectively; $p< 0.001$) (30).

When the HOMA-IR levels are compared, it was seen that the women and men of the METS group had the highest levels and it was found to be statistically significant (4.0±1.8 $p<0.0001$). The METS group had the highest insulin levels and it was statistically significant (16.3±7.7; $p<0.0001$). Also, there were significant positive correlations between HOMA-IR and BMI ($r=0.211$, $p<0.0001$), HOMA-IR and waistline ($r=0.264$, $p<0.0001$), HOMA-IR and hips ($r=0.203$, $p<0.0001$) and HOMA-IR and TSH levels ($r=0.286$, $p=0.001$).

A significant positive correlation was detected between uric acid and HOMA-IR ($r=0.262$, $p<0.0001$) and uric acid and insulin levels ($r=0.246$, $p<0.0001$). Upon comparing the uric acid levels of the groups, it was seen that the METS group had the highest levels of uric acid (5.2±1.2; $p<0.0001$). Upon comparing the genders, it was seen that the men with METS and DM had the highest levels.

In the study of Chen et al (31) on 78 adult female *Cynomolgus monkeys* to demonstrate the relationship between body weight and hematological and serum biochemical parameters using a multi-variant analysis, they reported that serum insulin levels increased with body weight; in addition, there was a correlation between insulin, GLU, Total Cholesterol and TG and also obesity in female *Cynomolgus monkeys* posed a high risk for DM, just like in humans. It is reported that 2 hematological parameters, RBC and MCV, are important for the increase in body weight in the multiple regression analysis and that body weight is

strongly related to leptin, insulin, RBC and MCV. Obese individuals usually spend more energy for their activities and use more oxygen. Chen's results show that obesity tends to increase blood parameters. This tendency shows itself as increased cardiac output and cardiomegaly in humans.

In the study of Demir et al (26) in which they compare healthy individuals to those with METS and DM, they did not detect a significant difference between the groups in terms of whole blood count parameters ($p>0.05$). The highest WBC levels were detected in the group with DM which complied with our previous studies but was not found to be statistically significant (7.6 ± 1.6; $p=0.353$). The HB and PLT levels were highest in the METS group but this was not statistically significant (HB and PLT levels respectively: 13.5 ± 1.4; $p=0.178$ and 294.0 ± 77.0; $p=0.194$).

As a result; the fact that we detected a significant positive correlation between HOMA-IR and TSH makes us think that high TSH levels may be a component of METS. The highest HOMA-IR, TG and insulin levels and the lowest HDL levels support the diagnosis. Also, the positive correlations between the waistline and hip circumference increase and SBP and DBP emphasize the importance of diet and exercise in obesity treatment. It must not be forgotten that thyroid dysfunction may be more commonly seen in obese, overweight and diabetic patients when compared to the normal population, so Family Medicine Physicians must be alert for thyroid dysfunction in obese patients. Despite the high incidence of thyroid nodules which were detected incidentally by USG, controlled studies with larger series are needed before we could suggest a "routine thyroid ultrasound practice in obese patients". Also, more studies are needed on the use of USG at primary care level and the education and application of USG should be extended and additionally newly equipping the Family Physicians should be aimed.

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REFERENCES:

1. Sağlık Bakanlığı Temel Sağlık Hizmetleri Genel Müdürlüğü, Beslenme ve Fiziksel Aktiviteler Daire Başkanlığı, Türkiye Obezite (Şişmanlık) İle Mücadele ve Kontrol Programı (2010-2014) Yayın No: 773, Ankara, TR: Sağlık Bakanlığı; 2011.
2. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Report on a WHO Consultation on Obesity, Geneva: WHO; 1998 Who/Nut/Ncd/98:1.
3. Kara İH, Baltaci D, Sayın S, et al. Investigation of hematological and biochemical parameters in obese women in reproductive age. Konuralp Tip Dergisi [Konuralp Medical Journal] 2012;4(1):1-7.
4. Biondi B. Thyroid and Obesity: An Intriguing Relationship. J Clin Endocrinol Metab. 2010;95(8):3614–7.
5. Yıldız S. Metabolik Sendromlu Hastalarda Visfatin Düzeyi. Düzce Üniversitesi Tıp Fakültesi İç Hastalıkları Anabilim Dalı, Uzmanlık Tezi, Düzce–2011.
6. İliçin G, Biberoğlu K, Süleymanlar G, Tiroid Hastalıkları. Editör: Ünal S. İç Hastalıkları 2. Baskı; Ankara: Güneş Kitabevi; 2003: 2276-88.
7. Koloğlu S. Diabetes Mellitus. Temel ve Klinik Endokrinoloji 1. Baskı. Ankara: Medikal Network ve Nobel; 1996:367-86.
8. Sencer E. Endokrinoloji Metabolizma ve Beslenme Hastalıkları. İstanbul: Nobel Tıp Kitabevi; 2001:274-89.
9. Baş M. Tip 2 Diabetik Kadınlarda Tiroid Fonksiyon Testleri ve Tiroid Ultrasonografisi. Sağlık Bakanlığı Taksim Eğitim ve Araştırma Hastanesi 1. Dâhiliye Kliniği. İstanbul: Uzmanlık Tezi; 2008.
10. Alexander C, Landsmann P, Teutsch S, et al. NCEP-Defined Metabolic Syndrome, Diabetes And Prevalence of Coronary Heart Disease Among NHANES III Participants Age 50 Years And Older. Diabetes 2003;52:1210–4.
11. National Institutes of Health: Third Report of the On Detection, Evaluation Treatment of High Blood Cholesterol in Adults. Adults Treatment Panel III. Executive Summary Bethesda, USA: National Institutes of Health; 2001.
12. Türkiye Endokrin ve Metabolizma Derneği. Obezite, Dislipidemi, Hipertansiyon Hekim İçin Tanı ve Tedavi Rehberi. Ankara: Türkiye Endokrin ve Metabolizma Derneği Yayınları; 2011.
13. Zinner M, Ashley S, Maingot S. Abdominal Operasyonlar. Ed. Andican A. Morbid Obezite ve Morbid Obezite Operasyonları; İstanbul: Nobel Tıp Kitapevi; 2007:455-60.
14. Aytürk S. Ötiroid Bireylerde Metabolik Sendrom Komponentleri İle Tiroid Fonksiyon, Volüm ve Nodül İlişkisi. Başkent Üniversitesi Tıp Fakültesi İç Hastalıkları Anabilim Dalı Endokrinoloji ve Metabolizma Hastalıkları Yan Dalı. Ankara: Uzmanlık Tezi; 2009.
15. Solbiati L, Charboneay W, Osti V, et al. The Thyroid Gland. Diagnostic Ultrasound. Editor: Johnson M. 3th. St. Louis. Missouri: Elsevier Mosby; 2005: 735–70.

16. Anderlova K, Křemen J, Doležalová R, et al. The influence of very-low-calorie-diet on serum leptin, soluble leptin receptor, adiponectin and resistin levels in obese women. Physiol Res 2006;55(3):277-83.
17. Lin SY, Wang YY, Liu PH, et al. Lower Serum Free Thyroxin levels are Associated with Metabolic Syndrome in a Chinese Population. Metabolism 2005;54(11):1524-8
18. Semiz S, Şenol U, Bircan O, et al. Correlation between age, body size and thyroid volume in an endemic area. J Endocrinol Invest 2001;24(8):559-63.
19. Ivarsson S, Persson P, Ericsson U. Thyroid gland volume as measured by ultrasonography in healthy children and adolescents in a non-iodine deficient area. Acta Paediatr Scand 1989;78(4):633-4.
20. Mohan S, Libanati C, Dony C, et al. Development, Validation, and Application of a Radioimmunoassay for İnsulin-Like Growth Factor Binding Protein-5 in Human Serum And Other Biological Fluids. J Clin Endocrinol Metab 1995;80(9):2638-45.
21. Santisteban P, Acebrón A, Polycarpou-Schwarz M, et al. Insulin and insulin- like growth factor 1 regulate a thyroid-specific nuclear protein that binds to the thyroglobulin promoter. Mol Endocrinol 1992;6(8):1310-7.
22. Vander J, Gaston E, Dawber T. The significance of nontoxic thyroid nodules: final report of a 15-year study of the incidence of thyroid malignancy. Annals of Internal Medicine 1998;69:537-40.
23. Erdogan M, Güllü S, Baskal N, et al. Omeprazole: Calcitonin Stimulation Test for the Diagnosis Follow-Up and Family Screening In Medullary Thyroid Carcinoma. J Clin Endocrinol Metab 1997,82(3):897–9.
24. Carpelli M. Morbid Obesity in Women is Associated to a Lower Prevalence of Thyroid Nodules. Obesity Surgery 2012;22(3):460-4.
25. Kömürcü T. Morbid Obez Hastalarda Tiroid Fonksiyonlarının Değerlendirilmesi. Sağlık Bakanlığı Ankara Atatürk Eğitim ve Araştırma Hastanesi Endokrinoloji ve Metabolizma Hastalıkları Kliniği Aile Hekimliği. Ankara: Uzmanlık Tezi; 2012.
26. Demir D, Bucaktepe G.E, Kara İH. Metabolik Sendrom, Tip 2 Diyabetes Mellitus ve Sağlıklı Bireylerin Sosyodemografik, Antropometrik ve Biyokimyasal Özelliklerinin Karşılaştırılması. Konuralp Tıp Dergisi [Konuralp Medical Journal] 2010;2(1):12-9.
27. Tanyeri F, Topbaş M, Dündar C ve ark. Samsun il merkezinde obezite prevalansı ve obezite arteriyel kan basıncı ilişkisi. Ondokuz Mayıs Üniversitesi Tıp Fakültesi Dergisi 2000;17(2): 69-77.
28. Özkan Y, Çolak R, Koca SS ve ark. Diyabet ve Hiperlipidemi: Tedavide Ne Kadar Başarılıyız? Fırat Ü. Sağlık Bilimleri Dergisi 2008;22(2):97-100.
29. Özinan M, Şentürk BA, Frenkçi S ve ark. Obez Kadınlarda İnsülin Direnci ve Serum Adiponektin Düzeyleri Arasındaki İlişki. Türk Klinik Biyokimya Dergisi 2008;6(2):51-7.
30. daSilva RC, Miranda WL, Chacra AR, Et al. Insulin resistance, beta-cell function, and glucose tolerance in Brazilian adolescents with obesity or risk factors for type 2 diabetes mellitus. J Diabetes Complications 2007;21(2):84-92.
31. Chen Y, Ono F, Yoshida T, et al. Relationship between Body Weight and Hematological and Serum Biochemical Parameters in Female Cynomolgus Monkeys. Exp Animal 2002;51(2):125-31.