RESEARCH ARTICLE

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# Evaluation of Plasma Ghrelin, Omentin–1 Levels and Insulin Resistance in Patients With Obstructive Sleep Apnea Syndrome

**ABSTRACT**

**Objective:** Available studies support the occurrence of a bidirectional association between obstructive sleep apnea syndrome (OSAS) and cardiovascular disorders. In this study, we aimed to evaluate the plasma ghrelin, omentin–1 levels, insulin resistance (IR) in patients with OSAS and its cardiovascular consequences.

**Methods:** This study was performed on 150 individuals who applied to the sleep laboratory with complaints such as snoring and sleep-breathing pause. Polysomnographic (PSG) evaluation was applied to every patient. Seventy five individuals with Apnea-Hypopnea Index (AHI) ≥5 were diagnosed as OSAS and seventy five individuals with AHI<5 were included as the without OSAS.

**Results:** The median omentin-1 level was 59.0 ng/mL in the OSAS group and 105.0 ng/mL in the without OSAS (p<0.001). The median ghrelin level in the OSAS group was 229.0 pg/ml and 180.0 pg/ml in the without OSAS group (p<0.001). The prevalence of OSAS was 2.667 times higher in males than females (OR=2.667). HOMA-IR scores were not different between OSAS and without OSAS groups (p=0.218). Patients with OSAS had higher BMI, neck circumference, and median ESS values compared to those of without OSAS group (p<0.001). In obese, the risk of OSAS was found 3.058 times higher (OR= 3.058) (p<0.001).

**Conclusions:** Median omentin-1 level was lower in the OSAS group than the without OSAS group, whereas median ghrelin level was higher in the OSAS and obese individuals. Due to the high prevalence of OSAS in hypertensive and obese individuals, effective screening, diagnosis, and treatment of OSAS are required to reduce cardiovascular risk.

**Keywords:** Obstructive Sleep Apnea Syndrome, Ghrelin, Omentin-1

# Obstrüktif Uyku Apne Sendromlu Hastalarda Plazma Ghrelin, Omentin-1 Düzeyleri ve İnsülin Dirençlerinin Değerlendirilmesi

**ÖZET**

**Amaç:** Mevcut çalışmalar, obstrüktif uyku apne sendromu (OUAS) ile kardiyovasküler bozukluklar arasında çift yönlü bir ilişki olmasını desteklemektedir. Bu çalışmada OUAS'lı hastalarda plazma ghrelin, omentin-1 düzeyleri, insülin direnci (IR) ve kardiyovasküler sonuçları değerlendirildi.

**Gereç ve Yöntem:** Bu çalışma uyku laboratuvarına horlama ve uykuda solunum duraklaması gibi şikayetlerle başvuran 150 kişi üzerinde gerçekleştirildi. Her hastaya polisomnografik (PSG) değerlendirme uygulandı. Apne-Hipopne İndeksi (AHI) ≥5 olan yetmiş beş hastaya OUAS tanısı konuldu ve AHI <5 olan yetmiş beş hasta OUAS olmayanlar olarak alındı.

**Bulgular:** Ortanca omentin-1 seviyesi OUAS grubunda 59,0 ng/mL ve OUAS olmayanlarda 105,0 ng/mL idi (p<0,001). OUAS'larda ortanca ghrelin seviyesi 229,0 pg/ml, OUAS olmayanlarda 180,0 pg/ml idi (p<0,001). OUAS prevalansı erkeklerde kadınlardan 2,667 kat daha fazla idi (OR=2,667). OUAS ile HOMA-IR skorları arasında bir fark bulunmadı (p=0,218). OUAS'lı hastalar OUAS olmayanlara göre daha yüksek BMI, boyun çevresi ve ortanca ESS değerlerine sahipti (p<0,001). Obezlerde OUAS riski 3,058 kat daha fazla bulundu (OR=3,058) (p<0,001).

**Sonuç:** OUAS olanlarda omentin-1 ortanca değerleri OUAS olmayanlardan daha düşük iken, OUAS ve obez bireylerde ortanca ghrelin düzeyi daha yüksekti. Hipertansif ve obez bireylerde OUAS prevalansının yüksek olmasından dolayı, kardiyovasküler riski azaltmak için bunlarda OUAS'ın etkili taraması, tanı ve tedavisi gereklidir.

**Anahtar Kelimeler:** Obstrüktif Uyku Apne Sendromu, Ghrelin, Omentin-1, Kardiyovasküler Risk

## INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a disease characterized by recurrent complete or partial obstructions in the upper respiratory tract during sleep (1). Dyslipidemia, hypertension, type 2 diabetes mellitus, cardiovascular and metabolic abnormalities are common in OSAS patients. OSAS and its cardiovascular consequences have been widely explored in observational and prospective studies. Most evidence verifies the positive relationship between OSAS and hypertension, coronary artery disease, atrial fibrillation, stroke and heart failure.

In non-obese OSAS patients/even in mild forms of sleep apnea, it has been shown to be associated with insulin resistance. OSAS was associated with significantly higher odds of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) after adjusting for age, gender and body mass index (BMI). OSAS-related factors that may contribute to metabolic dysregulation include increased sympathetic activity, due to sleep fragmentation, intermittent hypoxia and proinflammatory cytokine production (2-4). Causative mechanisms relating sleep problems to adverse health outcomes include reciprocal changes in circulating levels of leptin and ghrelin (5). These will increase appetite and calorie intake, reduce energy consumption, facilitate the development of obesity and increasing cardiovascular risk (6). Ghrelin is known as an endocrine pathway in the control of feeding behavior and energy balance. Ghrelin is a 28 amino acid hormone is secreted by many tissues, but its main source is the gastric mucosa. Active form of ghrelin is acylated ghrelin with some metabolic actions like stimulation the appetite, increase the secretion of growth hormone, decrease insulin secretion from the pancreas, reducing in energy consumption by the body and effects on growth and peripheral metabolism especially of fats and carbohydrates (7).

Visceral adipose tissue acts as an endocrine organ and secretes various adipocytokines one of them is omentin (8). Omentin increases insulin-mediated glucose uptake by adipocytes; omentin-1 plays an important role the regulating insulin and has beneficial effects on IR (9). Decreased levels of omentin-1 are also associated with insulin resistance, type 2 diabetes mellitus, coronary artery disease, arterial stiffness, carotid plaque or in other words correlated inversely with the metabolic syndrome (10,11).

In this study, we aimed to evaluate the plasma ghrelin, omentin–1 levels, insulin resistance (IR) in patients with OSAS and its cardiovascular consequences.

## MATERIAL AND METHODS

**Study Design, Setting, and Population:** This cross-sectional analytical typed study was conducted on adult subjects with and without OSAS who were admitted to the Sleep Disorder Clinic, Department of Pulmonary Diseases, Meram Medical Faculty, Necmettin Erbakan University between April 2014 and December 2014. This study was conducted in 150 adults over the age of 18 who applied to the sleep laboratory with complaints such as snoring and sleep-breathing pause that their partners witnessed, excessive daytime sleepiness, fatigue and headache. The patients were admitted randomly according to the order of application to the sleep laboratory on the specified dates. Polysomnographic (PSG) evaluation was applied to every patient who applies to the sleep laboratory. Seventy five individuals with Apnea-Hypopnea Index (AHI) $\geq 5$ were diagnosed as the OSAS group and 75 individuals with AHI<5 were included as the without OSAS group.

**Ethical Approval:** Ethical approval for the study was obtained from the Ethics Committee of Meram Faculty of Medicine, Konya Necmettin Erbakan University (approval number: 2014/44). The participants were informed about the study and their written and verbal consent was obtained according to the principles of Helsinki Declaration.

**Sampling Selection:** The prevalence of OSAS has been reported approximately as 3% (10). As the number of subjects in the target population for our investigation was unknown, the number of subjects who should be included in the investigation was calculated using the formula $n=t2.p.q/d^2$.

According to the AHI values, the participants were enrolled in the study, of which 75 were OSAS groups and 75 were without OSAS groups.

**Data Collection:** Sociodemographic characteristics, comorbid diseases, history of medication use, and smoking status were determined using a patient data form prepared previously according to the literature. All participants were administered the Epworth Sleepiness Scale (ESS) and then underwent standard overnight polysomnography (PSG) in the sleep laboratory.

**Exclusion Criteria:** Exclusion criteria were heart failure, chronic obstructive pulmonary disease, received a systemic steroid or hormone replacement treatment, hepatic or renal failure, anatomical anomalies affecting the respiratory tract, diabetes mellitus, parenchymal lung disease, active malignancy, those who had received medical and/or surgical treatment for a sleep disorder, and those who did not provide written consent to participate in the study.

**Anthropometric Measurements:** Height, weight, and neck circumference were measured. Neck circumference was measured at the level of the superior border of the cricothyroid membrane. Body mass index (BMI) was calculated by dividing

body weight in kilograms by the square of body height in meters and expressed as kg/m2. The subjects were classified as normal (BMI: 18.5–24.9), overweight (BMI: 25.0–29.9), and obese (BMI ≥ 30.0) (11).

**Polysomnographic Evaluation (PSG):** Standard overnight PSG was performed to every patient by using a digital PSG system (Somnoscreen plus, Somnomedics GmbH, Randersacker, Germany) in the sleep laboratory. Channels (C1A2, C2A1, O1A2, O2A1, F3A2, F4A1) electroencephalography, two-channels (right and left) electrooculography, and submental electromyography (EMG) probes were placed on the patients for the sleep evaluation. Nasal airflow was recorded by placing an oronasal flowmeter and thermistor into the nose, while thoracic and abdominal motion was recorded after inserting thoracoabdominal effort sensors. Additionally, hemoglobin oxygen saturation and heart beat rate were monitored using pulse oxymetry. Leg movement was recorded using an EMG sensor placed on the anterior tibialis muscle of one leg. Sleep stage and respiration events were scored manually in accordance with AASM scoring criteria (12).

A decrease in airflow by ≥ 90% according to ≥ 10 sec basal values with effort to continue breathing was accepted as obstructive apnea. Decreased airflow by ≥30% for ≥10 sec accompanied by ≥3% oxygen desaturation or arousal from sleep was evaluated as hypopnea. The OSAS diagnosis was established according to the symptom evaluation and results of the sleep tests together.

**Apnea-Hypopnea Index:** The AHI was calculated by dividing the total number of apnea and hypopnea episodes to sleep duration (per hour). Seventy five individuals with Apnea-Hypopnea Index (AHI) ≥5 were diagnosed as OSAS and seventy five individuals with AHI<5 were included as the without OSAS group. OSAS severity was classified based on AHI values, such that patients with AHI of 5–15, 16–30, and >30 were classified as mild, moderate, and severe OSAS, respectively (12,13).

**Epworth Sleepiness Scale (ESS):** The ESS is a simple and reliable test used to evaluate daytime sleepiness in adults. This test is composed of eight questions that query the likelihood of falling asleep when the subject is excessively tired. The answers given for each question are scored on a scale of 0–3 and a final score is obtained. Scores >10 are considered daytime sleepiness (14).

**Laboratory Evaluation:** The blood samples were obtained after PSG. Fasting blood glucose (FBG) and insulin levels were measured immediately after an overnight fast. Plasma samples to test the other parameters were stored at –80°C until testing. Omentin-1 and ghrelin levels were measured using enzyme-linked immunosorbent assays. The homeostatic model assessment of insulin resistance (HOMA-IR) value was calculated using the formula: HOMA-IR = FBG (mg/dL)×plasma insulin (μU/mL)/405. The threshold value for IR was >2.7.

**Statistical Analysis:** SPSS for Windows 20.0 software (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Descriptive statistics for continuous variables were given in terms of average and standard deviation, and descriptive statistics for categorical data were given in terms of frequency and percentage. The Kolmogorov–Smirnov test was used to compare quantitative data to a normal distribution. Since the data do not show to normal distribution; for statistical analysis of quantitative data, Mann Whitney U test was used in paired groups and Kruskall Wallis test was used in triple groups. Chi-square test was used to compare categorical data. Pearson correlation analysis was used for correlations between parameters. Correlation coefficients (r) of 0.00-0.24 were evaluated as weak relationships, 0.25-0.49 as moderate, 0.50-0.74 as strong, and 0.75-1.00 as very strong. Univariate and multivariate linear regression analysis was performed to determine the independent risk factors of dependent variable AHI. The results were evaluated with 95% confidence intervals and a significance level of $p<0.05$. .

## RESULTS

This study was conducted with 150 adult subjects comprised of 75 patients with OSAS and 75 subjects without OSAS. Of the OSAS participants; 16.7% (n = 25) were mild, 16.0% (n = 24) were moderate, and 17.3% (n = 26) were severe OSAS based on the AHI. Mean age of the OSAS group was 44.17±11.5 years and that of the without OSAS group was 34.1±12.2 years ($p<0.001$). If a median value of 38 years was the cut-off, the frequency of OSAS in patients aged ≥ 38 years was 70.0% (n=56) whereas that of those aged <38 years was 27.1% (n=19). The incidence of OSAS at ≥38 years was 6.263 times higher than that of patients < 38 years. [OR= 6.263; 95% CI, 3.075–12.758)].

The OSAS group was comprised of 48 males (61.5%) and 27 females (38.5%). The without OSAS group was comprised of 30 (38.5%) males and 45 (62.5%) females (Figure 1).

The prevalence of OSAS was 2.667 times greater in males than females [OR= 2.667; 95% CI, (1.378–5.160)] ($p=0.003$). No significant relation was found between smoking status and any parameters we examined including sleep parameters ($p>0.05$). OSAS was detected in 64 (92.8%) of the 69 subjects who received ESS ≥10 points, and five (7.2%) subjects did not have OSAS ($p<0.001$). Sociodemograhic characteristics of the participants were shown Table 1.

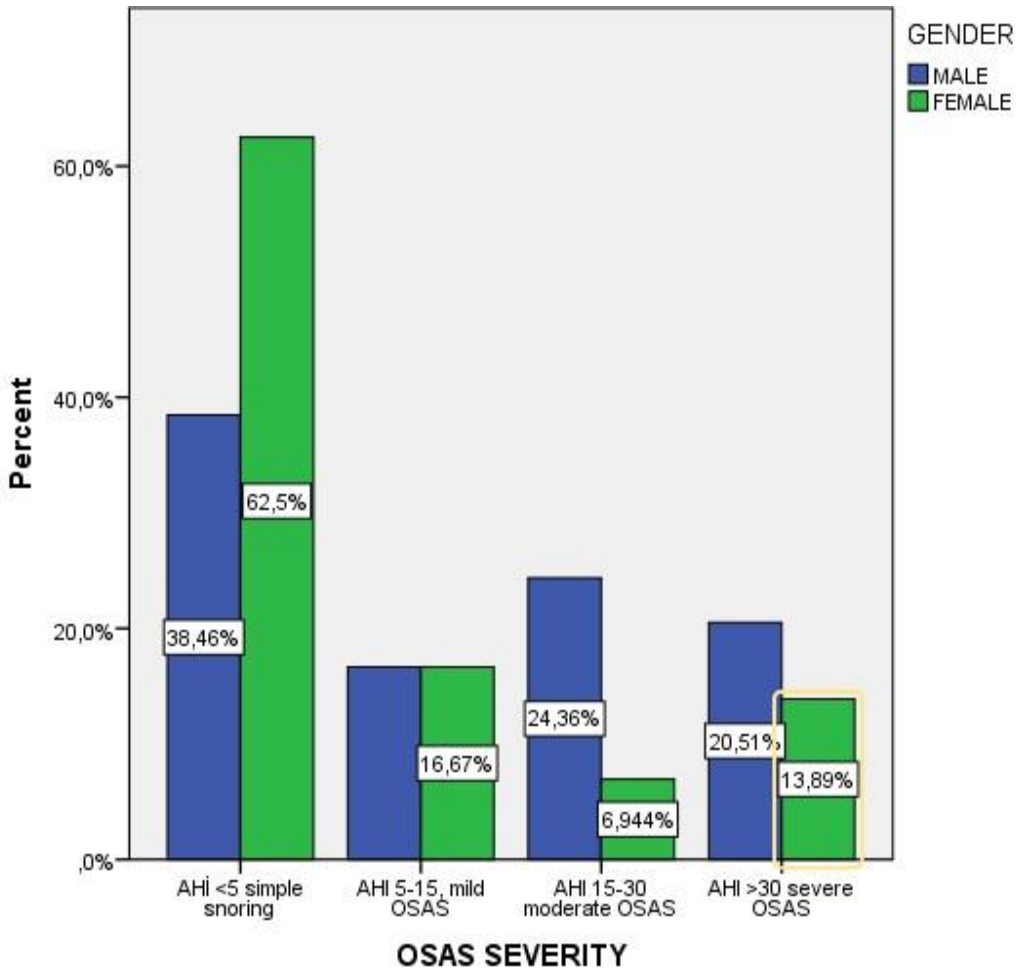


**Figure 1.** Relationship between OSAS severity and gender

**Table 1.** Sociodemograhic characteristics of the participants

| | With OSAS* | | Without OSAS | | | | |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | Total | $\chi^2$ | *p* |
| **Age** | | | | | | | |
| ≥38 years | 56 | 70.0 | 24 | 30.0 | 80 | 27.429 | **<0.001** |
| <38 years | 19 | 27.1 | 51 | 72.9 | 70 | | |
| **Gender** | | | | | | | |
| Female | 27 | 37.5 | 45 | 62.5 | 72 | 8.654 | **0.003** |
| Male | 48 | 61.5 | 30 | 38.5 | 78 | | |
| **Marital status** | | | | | | | |
| Married | 62 | 58.5 | 44 | 41.5 | 106 | 9.295 | **0.002** |
| Non-married | 13 | 29.5 | 31 | 70.5 | 44 | | |
| **Smoking status** | | | | | | | |
| Smokers | 30 | 53.6 | 26 | 46.4 | 56 | | |
| Non-smokers | 45 | 47.9 | 49 | 52.1 | 54 | 0.456 | 0.500 |
| **Education status** | | | | | | | |
| ≤Primary school educated | 18 | 60.0 | 12 | 40.0 | 30 | | |
| Secondary school educated | 12 | 66.7 | 6 | 33.3 | 18 | 0.276 | 0.871 |
| University-educated | 27 | 60.0 | 18 | 40.0 | 45 | | |
| **Epworth SS** | | | | | | | |
| ≥10 points | 64 | 92.8 | 5 | 7.2 | 69 | 93.425 | **<0.001** |
| < 10 points | 11 | 13.6 | 70 | 86.4 | 81 | | |

**OSAS*** Obstructive sleep apnea syndrome

Of the patients with OSAS, 14 (30.4%), 27 (50.0%), and 34 (68.0%) were normal weight, overweight, and obese, respectively, according to their BMI. Of the subjects in the without OSAS group; 32 (69.6%), 27 (50.0%), and 16 (32.0%) were normal weight, overweight, and obese,

respectively. In obese, the risk of OSAS was found 3.058 times higher than those who were not obese [OR= 3.058; 95% CI, (1.495–12.758)] (p<0.001).

The median omentin-1 level was found to be 59.0 (2-1163) ng/mL in the OSAS group and 105.0 (7-1464) ng/mL in the without OSAS group. There was a significant difference between the groups (p<0.001). The median value of ghrelin was 229.0 (62-5385) pg/ml in the OSAS group and 180.0 (31-3806) pg/ml in the without OSAS group. There was a significant difference between the groups (p<0.001). Patients with OSAS were older, and had higher BMI, neck circumference, and median ESS values but lower blood pressure compared to those of the without OSAS group (p<0.001) (Table 2).

**Table 2.** Comparison of some parameters in the two groups

| | **With OSAS** | **Without OSAS** | | |
|---|---|---|---|---|
| | **Median (min-max)** | **Median (min-max)** | **Z** | ***p**** |
| **Age (year)** | 47.0 (23-78) | 32.0 (19-70) | -5.397 | **<0.001** |
| **Systolic BP(mmHg)** | 130 (90-170) | 130 (120-140) | -2.001 | **0.045** |
| **Diastolic BP(mmHg)** | 80 (50-100) | 80 (60-90) | -3.947 | **<0.001** |
| **BMI (kg/m ²)** | 29.4(19.3-46.5) | 25.9(18.6-45.0) | -4.031 | **<0.001** |
| **Neck (cm)** | 38.0 (33-46) | 37.0 (34-45) | -5.568 | **<0.001** |
| **Epworth SS** | 14 (3-24) | 3 (0-15) | -9.816 | **<0.001** |
| **FBG (mg/dl)** | 95.0 (74-194) | 91.0 (70-136) | -2.782 | **0.005** |
| **Insulin (µ / ml)** | 8.1 (0.9-95) | 8.2(1.6-55.3) | -0.718 | 0.473 |
| **Omentin (ng/ml)** | 59.0 (2-1163) | 105.0 (7-1464) | -5.071 | **0.001** |
| **Ghrelin (pg/ml)** | 229.0 (62-5385) | 180.0 (31-3806) | -3.724 | **0.001** |
| **HOMA-IR** | 2.1(0.2-32.1) | 1.8(0.4-15.9) | -1.231 | 0.218 |
| **NREM** | 2.3 (0-28.5) | 3.9 (0-20.0) | -2.779 | **0.005** |
| **REM** | 3(0-20) | 6.0 (0-21.4) | -0.382 | 0.703 |
| **Min. $O_2$ sat.** | 83(50-91) | 89 (78-94) | -8.433 | **0.001** |
| **Average $O_2$ sat.** | 90(68-95) | 93 (18-98) | -4.347 | **0.001** |
| **≤ 90 $O_2$ sat.** | 23.9(0-99.8) | 2.1(0-9.1) | -8.131 | **0.001** |

***** Mann–Whitney *U*-test

Gender had no effect on blood pressure, FBG, insulin, omentin-1, ghrelin, HOMA-IR, or BMI values. Median age and neck circumference measurements were significantly higher in males than females (p=0.025 and p< 0.001, respectively).

Median AHI and ESS values were significantly higher in males compared to females (p=0.002, p=0.006, respectively). Non rapid eye movement sleep (NREM) was significantly longer in females than males (p=0.040). AHI, oxygen saturation ≤ 90%, and median ESS values increased significantly as BMI increased and minimum oxygen saturation decreased. Significant differences in NREM and REM sleep duration were observed between the groups.

BMI increased with age and, consequently, neck circumference, diastolic blood pressure, FBG, insulin, and HOMA-IR values increased significantly as BMI increased (Table 3). Correlation between Omentin-1, Ghrelin and some parameters in OSAS patients was shown in Table 4.

**Table 3.** The effects of body mass index (BMI) on some parameters

| | **Normal weight BMI:18.5–24.9kg/m²** | **Overweight BMI: 25.0–29.9 kg/m²** | **Obese BMI ≥ 30.0 kg/m²** | | |
|---|---|---|---|---|---|
| | **Median (min-max)** | **Median (min-max)** | **Median (min-max)** | **$\chi^2$** | ***p**** |
| **Age (year)** | 28.5 (19-59) | 38 (19-79) | 47 (21-78) | 23.22 | **0.001** |
| **Neck (cm)** | 36.5 (33-39.3) | 37.3 (34-44) | 38.5 (36.5-46) | 57.39 | **0.001** |
| **SBP (mmHg)** | 130 (120-140) | 130 (90-140) | 130 (110-170) | 20.55 | 0.151 |
| **DBP (mmHg)** | 80 (60-90) | 80 (50-90) | 80 (50-100) | 3.78 | **0.001** |
| **FBG (mg/dl)** | 90.5 (70-125) | 93 (74-194) | 99.5 (79-158) | 18.70 | **0.001** |
| **Insulin (µ/ml)** | 6.3 (1.6-30) | 7.6 (0.9-80.5) | 10.8 (3.6-95.4) | 10.05 | **0.007** |
| **Omentin (ng/ml)** | 99 (5-1464) | 89 (3-1375) | 75.5(2-1275) | 2.93 | 0.231 |
| **Ghrelin(pg/ml)** | 195.5 (62-4105) | 213.5 (31-5385) | 216 (102-4990) | 1.005 | 0.369 |
| **HOMA-IR** | 1.5 (0.4-7.1) | 1.7 (0.2-26.0) | 2.6 (1-32.1) | 12.31 | **0.002** |

* Kruskal–Wallis test

**Table 4.** Correlation between Omentin-1, Ghrelin and some parameters in OSAS patients.

| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|
| **1.Omentin-1** (ng /ml) | r | 1 | | | | | | | |
| | p | | | | | | | | |
| **2.Ghrelin** (pg/ml) | r | -.089 | 1 | | | | | | |
| | p | .450 | | | | | | | |
| **3.AHI** | r | .142 | -.010 | 1 | | | | | |
| | p | .224 | .932 | | | | | | |
| **4.HOMA-IR** | r | -.053 | -.049 | .196 | 1 | | | | |
| | p | .650 | .678 | .092 | | | | | |
| **5.BMI** ($kg/m^2$) | r | .089 | .012 | .238** | .100 | 1 | | | |
| | p | .450 | .920 | .040 | .394 | | | | |
| **6.ESS** | r | -.026 | .118 | .259 | .074 | .138 | 1 | | |
| | p | .827 | .312 | .025 | .528 | .239 | | | |
| **7.Min. $O_2$ sat.** | r | -.044 | .149 | -.523** | -.047 | -.299 | -.327 | 1 | |
| | p | .709 | .201 | .000 | .691 | .009 | .004 | | |
| **8. Aver. $O_2$ sat.** | r | -.065 | .173 | -.440** | .105 | -.166 | -.315 | .695** | 1 |
| | p | .582 | .138 | .000 | .371 | .155 | .006 | .000 | |
| **9. ≤ 90 $O_2$ sat.** | r | .184 | -.245** | .298 | -.151 | .251 | .214 | -.537** | -.732** |
| | p | .114 | .034 | .010 | .197 | .030 | .065 | .000 | .000 |

** Correlation significant at 0.01

Univariate and multivariate linear regression analysis was performed to determine the independent risk factors of dependent variable AHI in OSAS patients. According to the univariate model results, the effect of BMI on AHI was positive and statistically significant (β=0.238, p=0.040). One unit increase in BMI results in 23.8% increase in AHI. According to the results of multiple linear regression analysis, the effect of only Min. O2 sat. on AHI was found to be negative and statistically significant (β= -0.515, p<0.001). Linear regression analysis of variables for dependent variable AHI in OSAS patients was shown in Table 5.

**Table 5**. Linear regression analysis of variables for dependent variable AHI in OSAS patients

| | **One variable model** | | | | **Multivariate model (stepwise)** | | | |
|---|---|---|---|---|---|---|---|---|
| | **$R^2$** | **β** | **t** | **p** | **$R^2$** | **β** | **t** | **p** |
| **BMI** ($kg/m^2$) | 0.057 | 0.238 | 2.092 | **0.040** | | | | |
| **ESS** | 0.067 | 0.259 | 2.292 | **0.025** | | | | |
| **Min. $O_2$ sat.** | 0.274 | -0.523 | -5.244 | **<0.001** | 0.303 | -0.515 | -5.230 | **<0.001** |
| **Aver. $O_2$ sat.** | 0.194 | -0.440 | -4.188 | **<0.001** | | | | |
| **≤ 90 $O_2$ sat.** | 0.089 | 0.298 | 2.662 | **0.010** | | | | |
| **Omentin-1** (ng /ml) | 0.020 | 0.142 | 1.226 | 0.224 | | | | |
| **Ghrelin** (pg/ml) | -0.014 | -0.010 | -0.085 | 0.932 | | | | |
| **HOMA-IR** | 0.038 | 0.196 | 1.708 | 0.092 | | | | |

## DISCUSSION

There is an increasing evidence of association between OSAS and cardiovascular diseases. A strong relationship has been reported between OSAS and arterial hypertension, especially in patients with resistant hypertension. OSAS is a disease which progressively comes into prominence as its clinical outcomes and relationship with other systemic disorders become clarified and tends to increase in prevalence by age. Recent research has suggested that the effects of sleep apnea on insulin dynamics can be completely explained by obesity. Omentin-1 plays an important role regulating insulin and has beneficial effects on IR, and ghrelin, which affects appetite. The literature suggests that omentin-1 insufficiency and high ghrelin levels may be associated with glucose intolerance, MetS, obesity and cardiovascular abnormalities (15,16). In this study, the results were similar to the literature. Omentin-1 levels were significantly lower in patients with OSAS than those without OSAS. Decreased levels of omentin-1 are also associated with insulin resistance type 2 diabetes mellitus, coronary artery disease, arterial stiffness and carotid plaque or in other words correlated inversely with the metabolic syndrome (17,18). However, in our study, omentin-1 levels were not associated with BMI, AHI, ESS, HOMA-IR levels.

It has been suggested that ghrelin may be of pathophysiological importance in the development of IR (19). Serum ghrelin levels are lower in patients with type 2 diabetes mellitus or IR and obese person (19,20). However, relationship

between serum ghrelin level and OSAS is controversial. Harsh et al.(21) and Ursavas et al.(22) reported that ghrelin levels were significantly increased in the OSAS group. Similar to that study, ghrelin levels were also higher in our OSAS group than without OSAS group. In Harsh et al study, BMI and total body fat were shown as predictors of ghrelin levels in both OSAS patients and controls, the minimal O2 saturation was a significant predictor in OSAS patients but not in without OSAS group (21). Ursavas et al. reported that there was a significant relationship between serum ghrelin levels and AHI, ESS (22). In our study, there was no correlation between ghrelin levels and ESS, IR and BMI. Apneic episodes are generally terminated by an arousal (brief awakening) which results in fragmented sleep. These arousals are believed to be an important contributor to the symptoms of excessive daytime sleepiness (EDS) and the neurocognitive impairment seen in sleep apnea (22,23). Some, but not all, studies have indicated that sleep loss is associated with increased sympathetic nervous system outflow. Increased cardiac sympathovagal balance could also reflect decreased vagal activity, which could explain increased ghrelin levels. Several studies have shown that the vagal activity has a negative influence on ghrelin (24,25).

In this study, the insulin resistance in patients with OSAS was not significantly different from the non-OSAS subjects. Although FBG levels were higher in OSAS than in controls, no difference was found between insulin and HOMA-IR scores. A positive correlation was found between HOMA-IR scores and BMI, AHI, ESS. Similar to our study, Sharma et al. reported no differences in IR between an obese OSAS group and obese control group. They reported that metabolic abnormalities were due to obesity rather than OSAS (23). In addition, two other controlled studies suggested that the relation between sleep apnea and plasma insulin levels or insulin resistance reflected the known effects of obesity (24,25). Contrarily, Makino et al. analyzed 213 patients with mild, moderate, and severe OSAS based on the AHI to investigate the relationship between AHI level and IR. They reported that sleep-disordered breathing was associated with insulin resistance independent of obesity (26). Bulcun et al. (27) reported that there was no difference between OSAS and control groups on IR, but IR was associated with AHI, BMI, arousal index and ESS score. In a study in which the IR scores were higher in OSAS, it was related to the values of IR AHI and minimum oxygen saturation (4). These contradictory results reported for IR in OSAS are probably due to the heterologous disease of sleep apnea in terms of properties reported to be associated with insulin resistance.

In conclusion, elderly age, increased BMI and increased AHI are risk factors for high ESS scores; this is associated with a decrease in omentin-1 and an increase in ghrelin and IR. It has been suggested that ghrelin and omentin-1 may have a pathophysiological prescription in the development of IR. Presented study showed that omentin-1 levels were lower and ghrelin levels were higher in the patients with OSAS. There was no relationship between omentin-1 and ghreline levels and IR. The essential approach in preventing obesity is use of anti-obesity medications. In the recent years, use of anti-ghrelin vaccine is a topical issue. Because, obesity is defined by low growth hormone and ghrelin levels. This vaccine prevents weight gain by inhibiting transmission of “ghrelin” hormone which sends hunger signal to brain via circulation (28). All studies to be conducted regarding detailed examination of the relationship between obesity, insulin resistance and biochemical molecules and evaluation of the results; It will contribute positively to the fight against other obesity-related comorbid conditions such as OSAS. However, more studies are needed to better assess the impact of OSAS, and possible benefit of treatment with continuous positive airway pressure (CPAP) on dyslipidemia, type 2 diabetes, insulin resistance and cardiovascular mortality.

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